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FILE COVERS 1907 - 11 May 2005  VOL 142 ISS 20
FILE LAST UPDATED: 10 May 2005  (20050510/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

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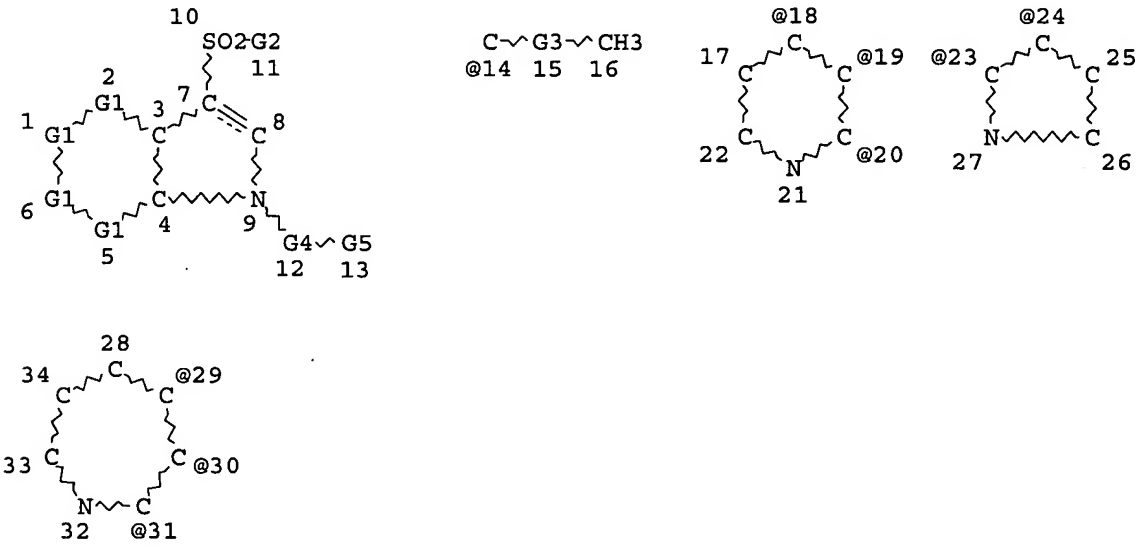


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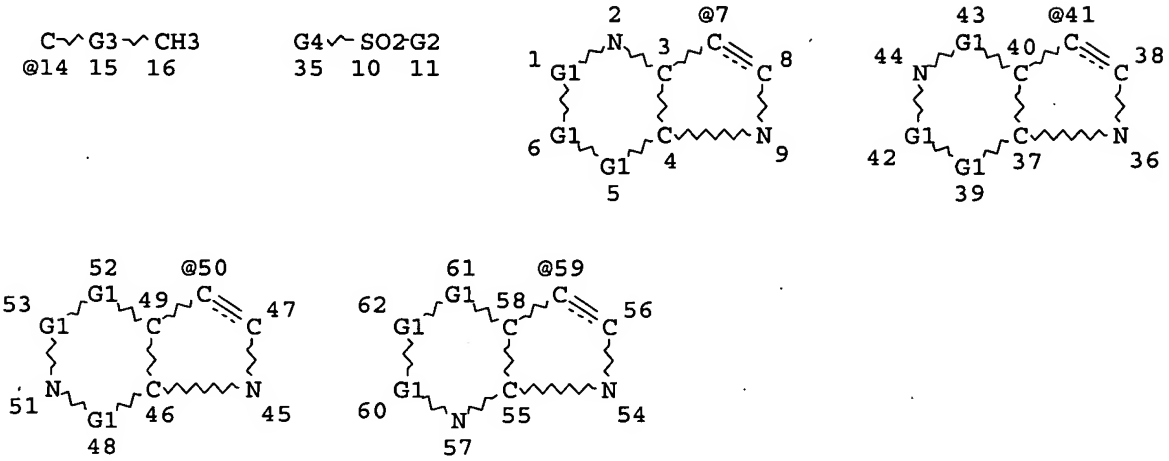

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L18 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:80697 HCAPLUS
DOCUMENT NUMBER: 140:146118
TITLE: Preparation of heterocyclylalkyl-sulfonylazaindole or -azaindazole derivatives 5-hydroxytryptamine-6 (5-HT6) ligands
INVENTOR(S): Bernotas, Ronald Charles; Lenicek, Steven Edward; Elokdah, Hassan Mahmoud; Li, David Zenan
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004009600	A1	20040129	WO 2003-US22506		20030717
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2491251	AA	20040129	CA 2003-2491251		20030717
US 2004023970	A1	20040205	US 2003-621432		20030717
PRIORITY APPLN. INFO.:			US 2002-396949P	P	20020718
			WO 2003-US22506	W	20030717

OTHER SOURCE(S): MARPAT 140:146118
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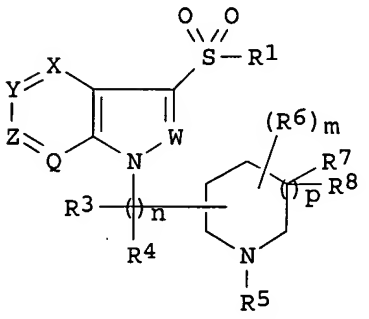

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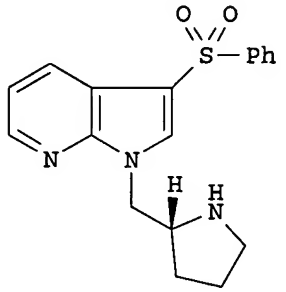


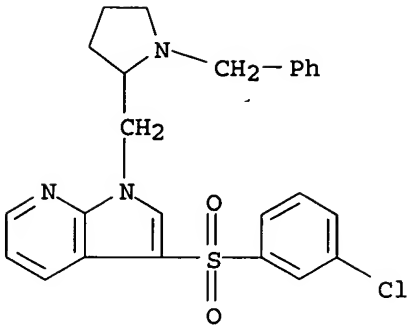
II

AB Title compds. I [W, X, Y, Z, Q = N, substituted C; R1 = (cyclo)alkyl, (hetero)aryl, etc.; R2 = H, halo, alkyl, alkoxy, etc.; R3-4 = H, alkyl; R5 = H, alk(en/yn)yl, etc.; R6 = alk(en/yn)yl, cycloalkyl, etc.; R7-8 = H, alk(en/yn)yl, cycloalkyl, etc.; m, n = 0-3; p = 0-2] are prepared For instance, 3-(Phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine (preparation given) is reacted with tert-Bu (2R)-2-[[[(4-methylphenyl)sulfonyl]oxy]methyl]-1-pyrrolidinecarboxylate (i. DMF, NaH, 0°; ii. dioxane, HCl, 4 h) to give II•HCl. II has Ki = 12 nM for the 5-HT6 receptor. I are useful for treatment of a central nervous system disorder related to or affected by the 5-HT6 receptor.

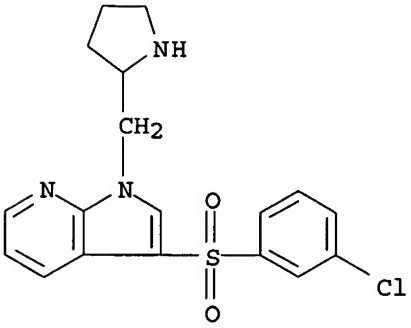
IT **651024-27-0P**, 1-[(1-Benzylpyrrolidin-2-yl)methyl]-3-(3-chlorophenylsulfonyl)pyrrolo[2,3-b]pyridine **651024-28-1P**, 3-(3-Chlorobenzenesulfonyl)-1-((pyrrolidin-2-yl)methyl)pyrrolo[2,3-b]pyridine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 1-heterocyclylalkyl-3-sulfonylazaindole or -azaindazole derivs. 5-hydroxytryptamine-6 (5-HT6) ligands)

RN 651024-27-0 HCAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine, 3-[(3-chlorophenyl)sulfonyl]-1-[[1-(phenylmethyl)-2-pyrrolidinyl]methyl]- (9CI) (CA INDEX NAME)



RN 651024-28-1 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-[(3-chlorophenyl)sulfonyl]-1-(2-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)



IT **651024-24-7P**, (-)-(R)-3-(Phenylsulfonyl)-1-(pyrrolidin-2-ylmethyl)pyrrolo[2,3-b]pyridine hydrochloride **651024-25-8P**, (+)-(S)-3-(Phenylsulfonyl)-1-(pyrrolidin-2-ylmethyl)pyrrolo[2,3-b]pyridine Hydrochloride **651024-29-2P**, 3-(3-Chlorophenylsulfonyl)-1-[(1-methylpyrrolidin-2-yl)methyl]pyrrolo[2,3-b]pyridine hydrochloride **651024-30-5P**, 3-(Phenylsulfonyl)-1-[(1-benzylpyrrolidin-2-yl)methyl]pyrrolo[2,3-b]pyridine hydrochloride **651024-31-6P**, 3-(3-Fluorophenylsulfonyl)-1-[(1-benzylpyrrolidin-2-yl)methyl]pyrrolo[2,3-b]pyridine hydrochloride **651024-32-7P**, 3-(3-Fluorophenylsulfonyl)-1-[(pyrrolidin-2-yl)methyl]pyrrolo[2,3-b]pyridine hydrochloride **651024-33-8P**, 3-(3-Fluorophenylsulfonyl)-1-[(1-methylpyrrolidin-2-yl)methyl]pyrrolo[2,3-b]pyridine hydrochloride **651024-34-9P**, 3-[(6-Chloroimidazo[2,1-b]thiazol-5-yl)sulfonyl]-1-[(1-benzylpyrrolidin-2-yl)methyl]pyrrolo[2,3-b]pyridine **651024-35-0P**, 3-[(6-Chloroimidazo[2,1-b]thiazol-5-yl)sulfonyl]-1-[(pyrrolidin-2-yl)methyl]pyrrolo[2,3-b]pyridine hydrochloride **651024-36-1P**, 3-[(5-Chlorothiophen-2-yl)sulfonyl]-1-[(pyrrolidin-2-yl)methyl]pyrrolo[2,3-b]pyridine hydrochloride **651024-37-2P**, 3-[(5-Chlorothiophen-2-yl)sulfonyl]-1-[(1-benzylpyrrolidin-2-yl)methyl]pyrrolo[2,3-b]pyridine hydrochloride **651024-40-7P**, 3-[(6-Chloroimidazo[2,1-b]thiazol-5-yl)sulfonyl]-1-(1-methylpiperidin-3-yl)pyrrolo[2,3-b]pyridine **651024-41-8P**, 3-[(4-Methylphenyl)sulfonyl]-1-((piperidin-4-yl)methyl)pyrrolo[2,3-b]pyridine **651024-42-9P**, 7-Methoxy-3-(phenylsulfonyl)-1-(piperidin-4-ylmethyl)pyrrolo[2,3-c]pyridine **651024-43-0P**,

6-Hydroxy-3-(phenylsulfonyl)-1-(piperidin-4-ylmethyl)-1H-pyrrolo[3,2-b]pyridine **651024-44-1P**, 6-Fluoro-3-[(3-fluorophenyl)sulfonyl]-1-((piperidin-4-yl)methyl)-1H-pyrrolo[3,2-b]pyridine **651024-45-2P**, 3-[(2-Fluorophenyl)sulfonyl]-6-methoxy-1-((piperidin-4-yl)methyl)-1H-pyrrolo[3,2-b]pyridine **651024-46-3P**, 4-Chloro-3-(phenylsulfonyl)-1-(piperidin-3-ylmethyl)pyrrolo[2,3-b]pyridine **651024-47-4P**, 7-Methoxy-3-(phenylsulfonyl)-1-(piperidin-3-ylmethyl)pyrrolo[2,3-c]pyridine **651024-48-5P**, 6-Hydroxy-3-(phenylsulfonyl)-1-(piperidin-3-ylmethyl)-1H-pyrrolo[3,2-b]pyridine **651024-49-6P**, 6-Chloro-3-[(4-fluorophenyl)sulfonyl]-1-((piperidin-2-yl)methyl)-1H-pyrrolo[3,2-c]pyridine **651024-50-9P**, 6-Fluoro-3-[(3-fluorophenyl)sulfonyl]-1-((piperidin-2-yl)methyl)pyrrolo[2,3-b]pyridine **651024-51-0P**, 5-Chloro-3-[(3-chlorophenyl)sulfonyl]-1-((piperidin-2-yl)methyl)pyrrolo[2,3-c]pyridine **651024-52-1P**, 3-[(2-Chlorophenyl)sulfonyl]-6-fluoro-1-((piperidin-2-yl)methyl)-1H-pyrrolo[3,2-b]pyridine **651024-53-2P**, 3-[(2-Fluorophenyl)sulfonyl]-6-methoxy-1-((piperidin-2-yl)methyl)-1H-pyrrolo[3,2-c]pyridine **651024-59-8P**, 6-Bromo-3-(phenylsulfonyl)-1-(pyrrolidin-3-ylmethyl)-1H-pyrrolo[3,2-c]pyridine **651024-60-1P**, 4-Chloro-2-methyl-3-(phenylsulfonyl)-1-(pyrrolidin-2-ylmethyl)pyrrolo[2,3-b]pyridine **651024-61-2P**, 7-Methoxy-3-(phenylsulfonyl)-1-(pyrrolidin-2-ylmethyl)pyrrolo[2,3-c]pyridine **651024-62-3P**, 6-Hydroxy-3-(phenylsulfonyl)-1-(pyrrolidin-2-ylmethyl)-1H-pyrrolo[3,2-b]pyridine **651024-63-4P**, 1-(Piperidin-2-ylmethyl)-3-(2-pyridinylsulfonyl)-1H-pyrrolo[3,2-c]pyridine **651024-64-5P**, 1-(Piperidin-3-ylmethyl)-3-(2-pyridinylsulfonyl)pyrrolo[2,3-b]pyridine **651024-65-6P**, 3-(2-Pyridinylsulfonyl)-1-((pyrrolidin-3-yl)methyl)pyrrolo[2,3-c]pyridine **651024-71-4P**, 1-(1-Phenethylpyrrolidin-3-yl)-3-(phenylsulfonyl)-1H-pyrrolo[3,2-c]pyridine **651024-72-5P**, 1-Piperidin-4-yl-3-(2-pyridylsulfonyl)pyrrolo[2,3-c]pyridine **651024-73-6P**, 1-Piperidin-3-yl-3-(2-thienylsulfonyl)-1H-pyrrolo[3,2-b]pyridine **651024-74-7P**, 1-Pyrrolidin-3-yl-3-(3-thienylsulfonyl)-1H-pyrrolo[3,2-b]pyridine **651024-75-8P**, 1-[(1-Benzylpyrrolidin-2-yl)methyl]-3-(phenylsulfonyl)pyrrolo[2,3-b]pyridine **651024-76-9P**, 3-(Phenylsulfonyl)-1-(pyrrolidin-2-ylmethyl)pyrrolo[2,3-b]pyridine **651024-77-0P**, 1-[(1-Benzylpyrrolidin-2-yl)methyl]-3-(3-fluorophenylsulfonyl)pyrrolo[2,3-b]pyridine **651024-78-1P**, 3-(3-Fluorophenylsulfonyl)-1-((pyrrolidin-2-yl)methyl)pyrrolo[2,3-b]pyridine **651024-79-2P**, 3-(3-Chlorophenylsulfonyl)-1-[(1-methylpyrrolidin-2-yl)methyl]pyrrolo[2,3-b]pyridine **651024-80-5P**, 3-[(6-Chloroimidazo[2,1-b][1,3]thiazol-5-yl)sulfonyl]-1-(pyrrolidin-2-ylmethyl)pyrrolo[2,3-b]pyridine **651024-81-6P**, 3-[(6-Chloroimidazo[2,1-b][1,3]thiazol-5-yl)sulfonyl]-1-(piperidin-3-yl)pyrrolo[2,3-b]pyridine **651024-82-7P**, 3-[(5-Chlorothiophen-2-yl)sulfonyl]-1-((pyrrolidin-2-yl)methyl)pyrrolo[2,3-b]pyridine **651310-86-0P 651310-90-6P**

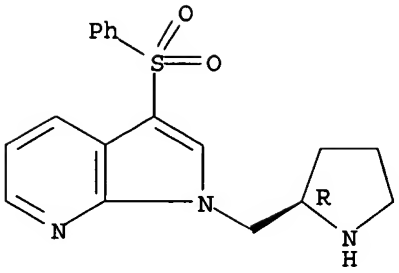
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 1-heterocyclylalkyl-3-sulfonylazaindole or -azaindazole derivs. 5-hydroxytryptamine-6 (5-HT6) ligands)

RN 651024-24-7 HCAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine, 3-(phenylsulfonyl)-1-[(2R)-2-pyrrolidinylmethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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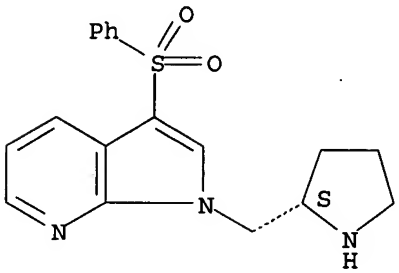
RN 651024-25-8 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-(phenylsulfonyl)-1-[(2S)-2-pyrrolidinylmethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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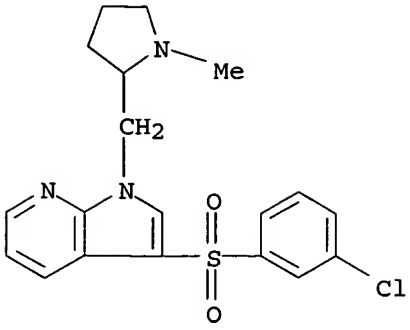

● HCl

RN 651024-30-5 HCAPLUS
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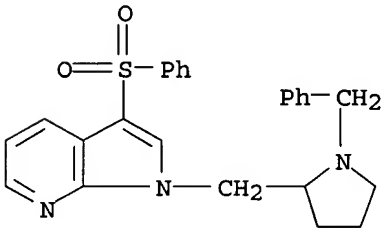

● HCl

RN 651024-31-6 HCAPLUS
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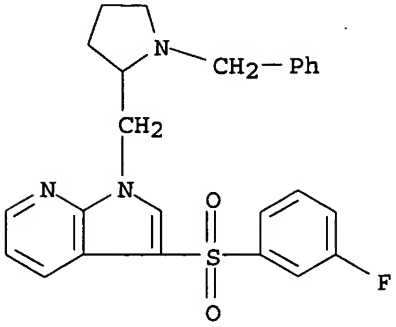

● HCl

RN 651024-32-7 HCAPLUS
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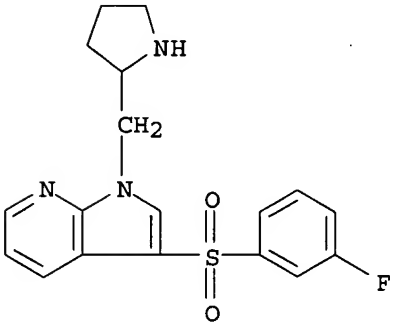
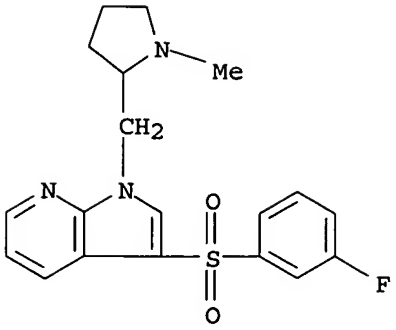


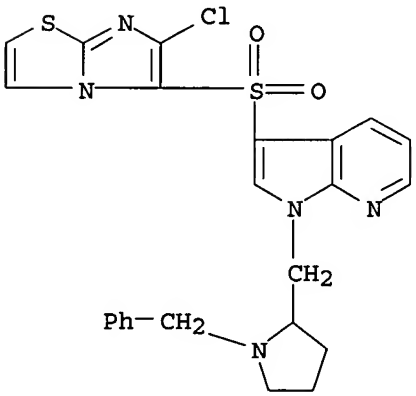
● HCl

RN 651024-33-8 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-[(3-fluorophenyl)sulfonyl]-1-[(1-methyl-2-pyrrolidinyl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

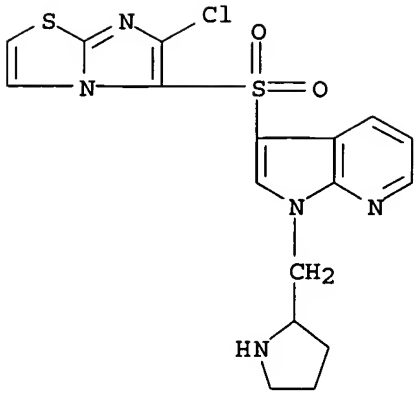


● HCl

RN 651024-34-9 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-[(6-chloroimidazo[2,1-b]thiazol-5-yl)sulfonyl]-1-[[1-(phenylmethyl)-2-pyrrolidinyl]methyl]- (9CI) (CA INDEX NAME)



RN 651024-35-0 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-[(6-chloroimidazo[2,1-b]thiazol-5-yl)sulfonyl]-1-(2-pyrrolidinylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



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RN 651024-36-1 HCAPLUS
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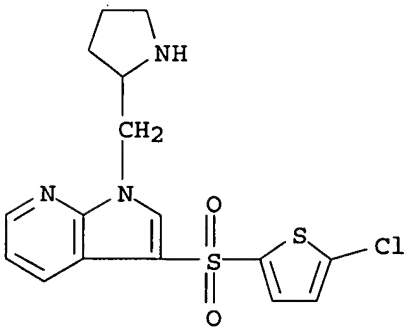

● HCl

RN 651024-37-2 HCAPLUS
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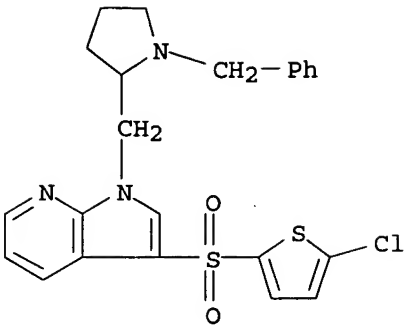

● HCl

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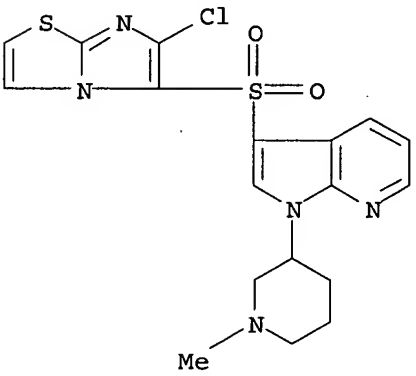

RN 651024-41-8 HCAPLUS
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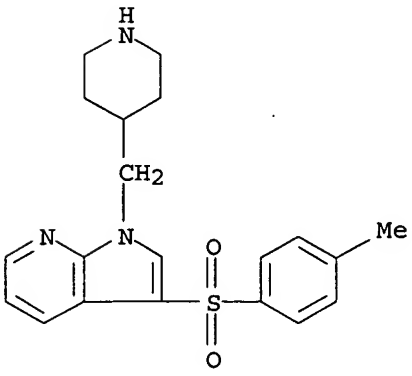

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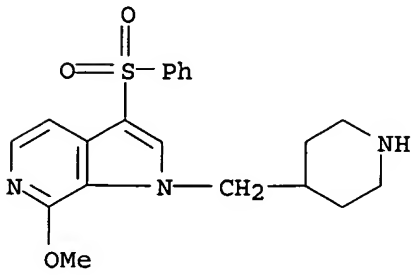
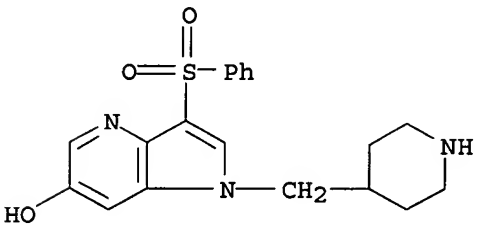
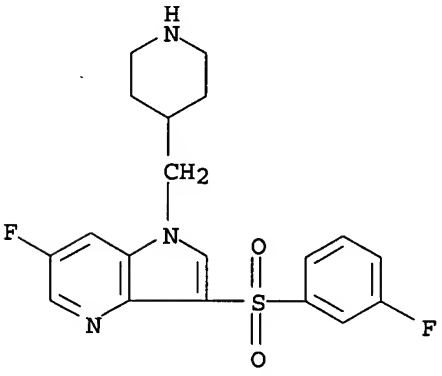


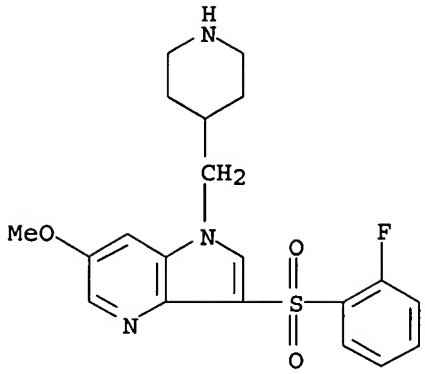
RN 651024-43-0 HCAPLUS
CN 1H-Pyrrolo[3,2-b]pyridin-6-ol, 3-(phenylsulfonyl)-1-(4-piperidinylmethyl)- (9CI) (CA INDEX NAME)



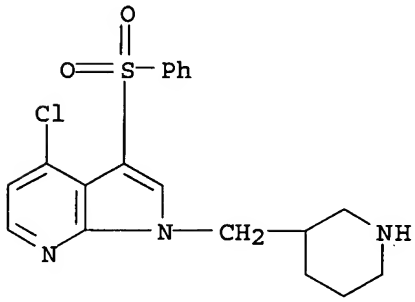
RN 651024-44-1 HCAPLUS
CN 1H-Pyrrolo[3,2-b]pyridine, 6-fluoro-3-[(3-fluorophenyl)sulfonyl]-1-(4-piperidinylmethyl)- (9CI) (CA INDEX NAME)



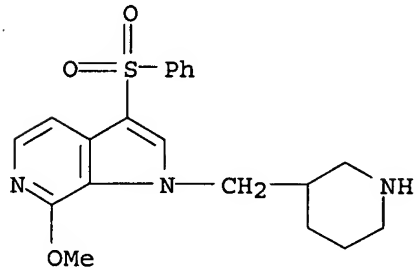
RN 651024-45-2 HCAPLUS
CN 1H-Pyrrolo[3,2-b]pyridine, 3-[(2-fluorophenyl)sulfonyl]-6-methoxy-1-(4-piperidinylmethyl)- (9CI) (CA INDEX NAME)



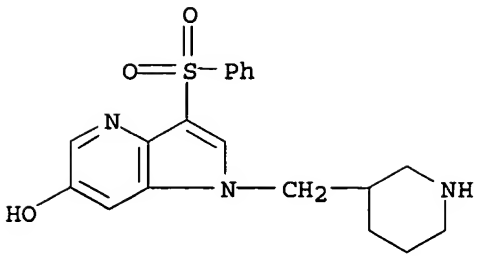
RN 651024-46-3 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 4-chloro-3-(phenylsulfonyl)-1-(3-piperidinylmethyl)- (9CI) (CA INDEX NAME)



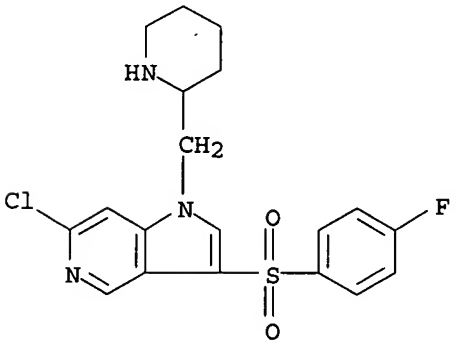
RN 651024-47-4 HCAPLUS
CN 1H-Pyrrolo[2,3-c]pyridine, 7-methoxy-3-(phenylsulfonyl)-1-(3-piperidinylmethyl)- (9CI) (CA INDEX NAME)



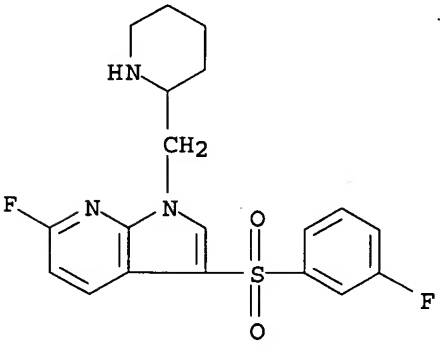
RN 651024-48-5 HCAPLUS
CN 1H-Pyrrolo[3,2-b]pyridin-6-ol, 3-(phenylsulfonyl)-1-(3-piperidinylmethyl)- (9CI) (CA INDEX NAME)



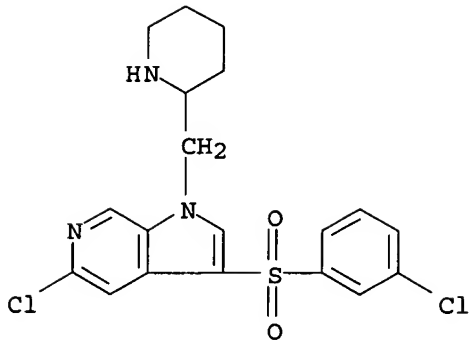
RN 651024-49-6 HCAPLUS
CN 1H-Pyrrolo[3,2-c]pyridine, 6-chloro-3-[(4-fluorophenyl)sulfonyl]-1-(2-piperidinylmethyl)- (9CI) (CA INDEX NAME)



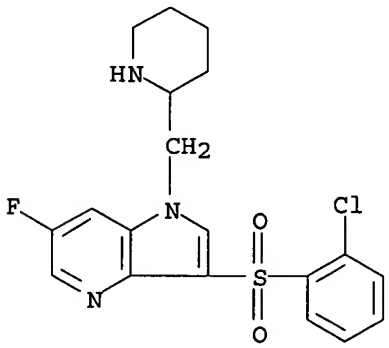
RN 651024-50-9 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 6-fluoro-3-[(3-fluorophenyl)sulfonyl]-1-(2-piperidinylmethyl)- (9CI) (CA INDEX NAME)



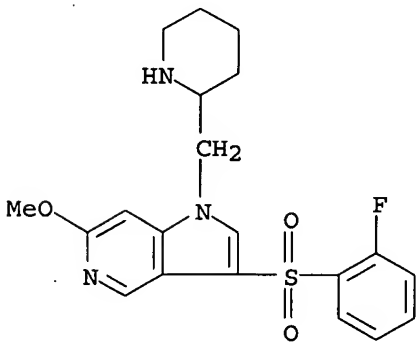
RN 651024-51-0 HCAPLUS
CN 1H-Pyrrolo[2,3-c]pyridine, 5-chloro-3-[(3-chlorophenyl)sulfonyl]-1-(2-piperidinylmethyl)- (9CI) (CA INDEX NAME)



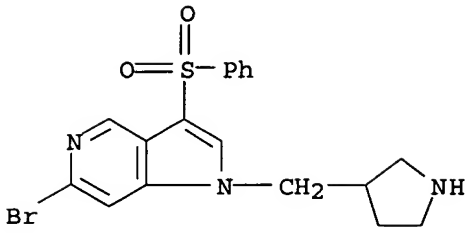
RN 651024-52-1 HCAPLUS
CN 1H-Pyrrolo[3,2-b]pyridine, 3-[(2-chlorophenyl)sulfonyl]-6-fluoro-1-(2-piperidinylmethyl)- (9CI) (CA INDEX NAME)



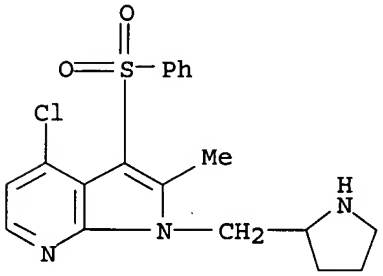
RN 651024-53-2 HCAPLUS
CN 1H-Pyrrolo[3,2-c]pyridine, 3-[(2-fluorophenyl)sulfonyl]-6-methoxy-1-(2-piperidinylmethyl)- (9CI) (CA INDEX NAME)



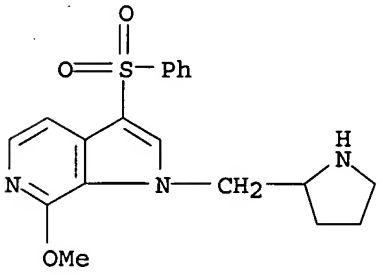
RN 651024-59-8 HCAPLUS
CN 1H-Pyrrolo[3,2-c]pyridine, 6-bromo-3-(phenylsulfonyl)-1-(3-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)



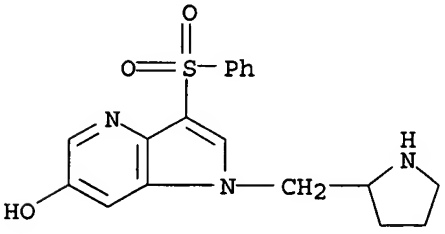
RN 651024-60-1 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 4-chloro-2-methyl-3-(phenylsulfonyl)-1-(2-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)



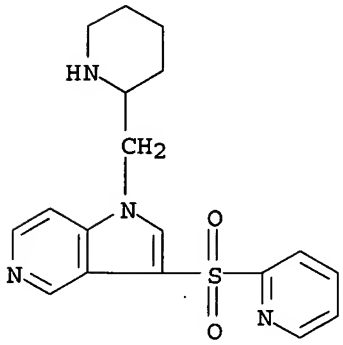
RN 651024-61-2 HCAPLUS
CN 1H-Pyrrolo[2,3-c]pyridine, 7-methoxy-3-(phenylsulfonyl)-1-(2-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)



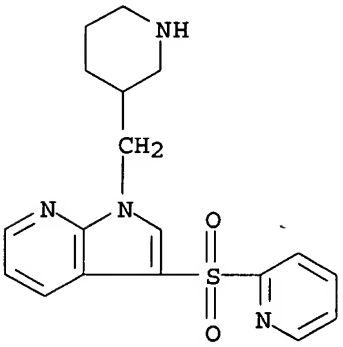
RN 651024-62-3 HCAPLUS
CN 1H-Pyrrolo[3,2-b]pyridin-6-ol, 3-(phenylsulfonyl)-1-(2-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)



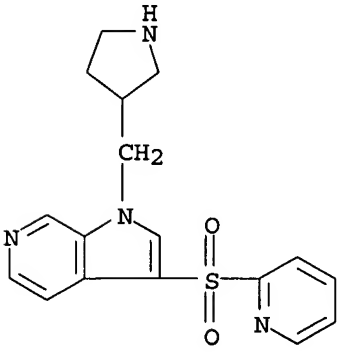
RN 651024-63-4 HCAPLUS
CN 1H-Pyrrolo[3,2-c]pyridine, 1-(2-piperidinylmethyl)-3-(2-pyridinylsulfonyl)- (9CI) (CA INDEX NAME)



RN 651024-64-5 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 1-(3-piperidinylmethyl)-3-(2-pyridinylsulfonyl)- (9CI) (CA INDEX NAME)

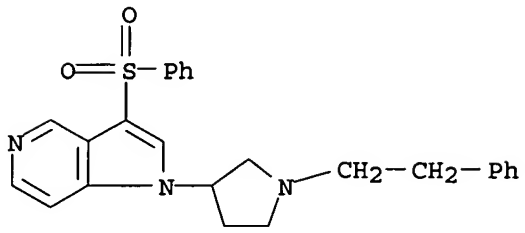


RN 651024-65-6 HCAPLUS
CN 1H-Pyrrolo[2,3-c]pyridine, 3-(2-pyridinylsulfonyl)-1-(3-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)

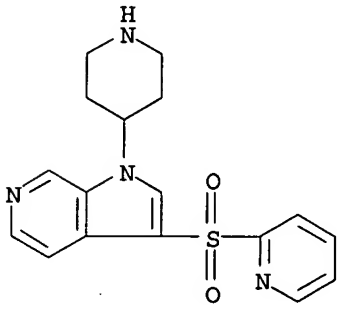


RN 651024-71-4 HCAPLUS
CN 1H-Pyrrolo[3,2-c]pyridine, 1-[1-(2-phenylethyl)-3-pyrrolidinyl]-3-

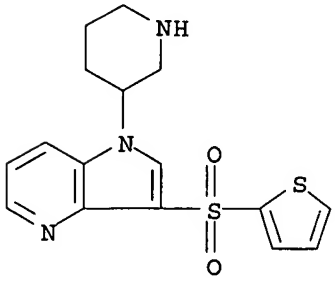
(phenylsulfonyl)- (9CI) (CA INDEX NAME)



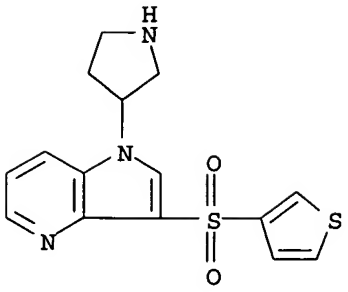
RN 651024-72-5 HCAPLUS
CN 1H-Pyrrolo[2,3-c]pyridine, 1-(4-piperidinyl)-3-(2-pyridinylsulfonyl)- (9CI) (CA INDEX NAME)



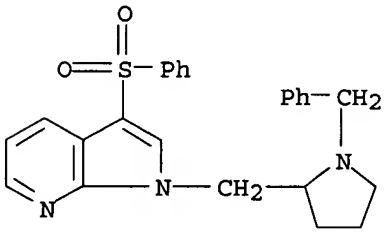
RN 651024-73-6 HCAPLUS
CN 1H-Pyrrolo[3,2-b]pyridine, 1-(3-piperidinyl)-3-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)



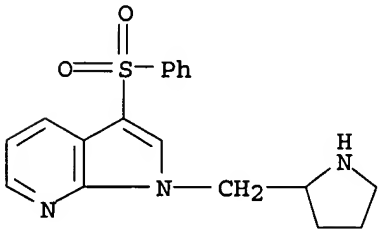
RN 651024-74-7 HCAPLUS
CN 1H-Pyrrolo[3,2-b]pyridine, 1-(3-pyrrolidinyl)-3-(3-thienylsulfonyl)- (9CI) (CA INDEX NAME)



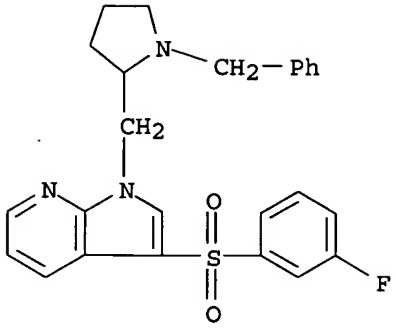
RN 651024-75-8 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 1-[[1-(phenylmethyl)-2-pyrrolidinyl]methyl]-3-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



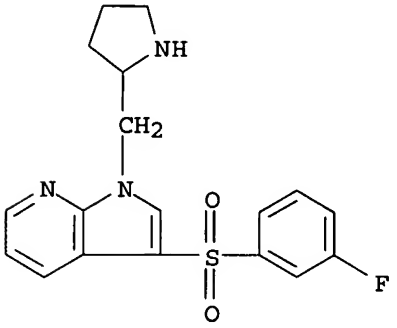
RN 651024-76-9 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-(phenylsulfonyl)-1-(2-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)



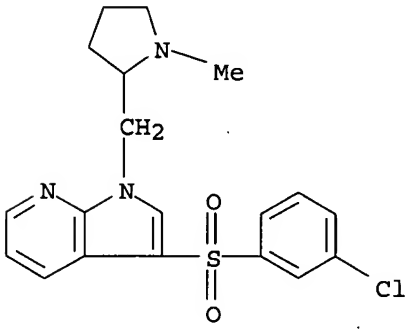
RN 651024-77-0 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-[(3-fluorophenyl)sulfonyl]-1-[[1-(phenylmethyl)-2-pyrrolidinyl]methyl]- (9CI) (CA INDEX NAME)



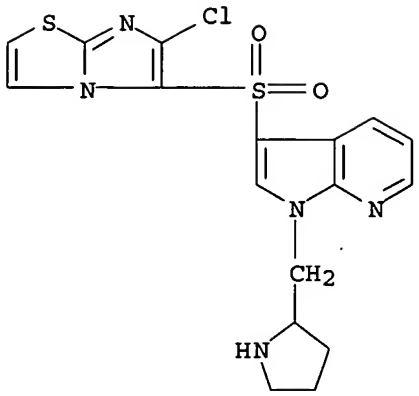
RN 651024-78-1 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-[(3-fluorophenyl)sulfonyl]-1-(2-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)



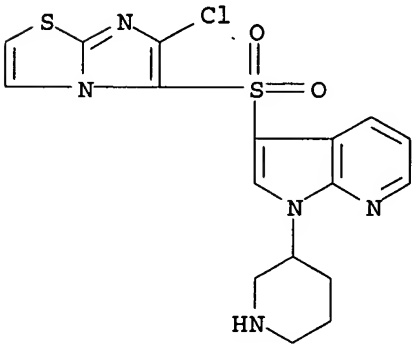
RN 651024-79-2 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-[(3-chlorophenyl)sulfonyl]-1-[(1-methyl-2-pyrrolidinyl)methyl]- (9CI) (CA INDEX NAME)



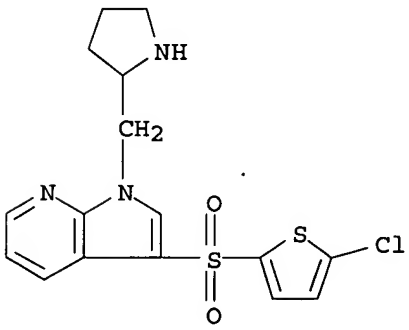
RN 651024-80-5 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-[(6-chloroimidazo[2,1-b]thiazol-5-yl)sulfonyl]-1-(2-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)



RN 651024-81-6 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-[(6-chloroimidazo[2,1-b]thiazol-5-yl)sulfonyl]-1-(3-piperidinyl)- (9CI) (CA INDEX NAME)

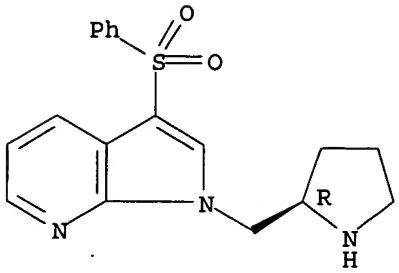


RN 651024-82-7 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-[(5-chloro-2-thienyl)sulfonyl]-1-(2-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)



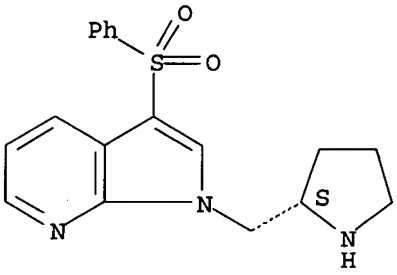
RN 651310-86-0 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-(phenylsulfonyl)-1-[(2R)-2-pyrrolidinylmethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 651310-90-6 HCAPLUS
CN 1H-Pyrrolo[2,3-b]pyridine, 3-(phenylsulfonyl)-1-[(2S)-2-pyrrolidinylmethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d stat que
L25 52 SEA FILE=HCAPLUS ABB=ON PLU=ON ("BERNOTAS R"/AU OR "BERNOTAS ROKAS"/AU OR "BERNOTAS RONALD"/AU OR "BERNOTAS RONALD C"/AU OR "BERNOTAS RONALD CHARLES"/AU)

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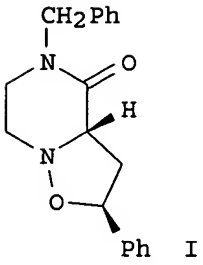
=> d ibib abs l25 1-52

L25 ANSWER 1 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:183904 HCAPLUS
TITLE: Diastereoselectivity in the cycloaddition of 1-benzyl-2-piperazinone nitrone with alkenes
AUTHOR(S): **Bernotas, Ronald C.**; Sing, Lily; Friedrich, Dirk
CORPORATE SOURCE: Aventis Pharmaceuticals, Bridgewater, NJ, 08807, USA
SOURCE: Synthesis (2005), (3), 465-469
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

GI



Ph I

AB The diastereoselectivity of the [2 + 3]-cycloaddn. of 1-benzyl-2-piperazinone nitrone with several alkenes has been examined Exo-Type cycloadducts, e.g., I, predominated for most substrates.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:130297 HCAPLUS
DOCUMENT NUMBER: 142:373637
TITLE: 4-(2-Aminoethoxy)-N-(phenylsulfonyl)indoles as novel 5-HT6 receptor ligands
AUTHOR(S): Zhou, Ping; Yan, Yinfa; **Bernotas, Ronald**; Harrison, Boyd L.; Huryn, Donna; Robichaud, Albert J.; Zhang, Guo Ming; Smith, Deborah L.; Schechter, Lee E.
CORPORATE SOURCE: Chemical and Screening Science and Neuroscience Discovery Research, Wyeth Research, Princeton, NJ, 08543-8000, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(5), 1393-1396
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The preparation of a novel class of 4-(2-aminoethoxy)-N-(phenylsulfonyl)indoles which exhibit high affinity towards the 5-HT6 receptor is reported here. Among these compds., 4-(2-methylaminoethoxy)-N-(phenylsulfonyl)indole showed superior affinity (Ki = 1 nM) towards the 5-HT6 receptor as well as excellent selectivity (>2000-fold) against the closely related subtype 5-HT7 receptor.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

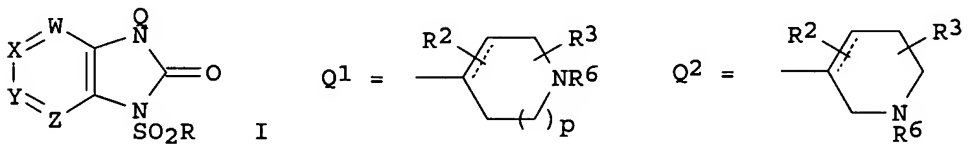
L25 ANSWER 3 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:78234 HCAPLUS
DOCUMENT NUMBER: 142:176841
TITLE: Preparation of sulfonyldihydroimidazopyridinones as serotonin 5-HT6 ligands
INVENTOR(S): Cole, Derek Cecil; **Bernotas, Ronald Charles**
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005020596	A1	20050127	US 2004-896832	20040722
WO 2005010003	A1	20050203	WO 2004-US23221	20040719

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-489416P P 20030723
OTHER SOURCE(S): MARPAT 142:176841
GI



AB Title compds. [I; Q = (CR2R3)nNR4R5, Q1, Q2; W = CR1, N; X = CR7, N; Y = CR8, N; Z = CR9, N; R = (substituted) cycloalkyl, aryl, heteroaryl, N-bridgehead bicyclyl, tricyclyl; R1, R7, R8, R9 = H, halo, cyano, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl; R2, R3 = H, (substituted) alkyl; n = 2-5; p = 0-2; R4, R5 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl; NR4R5 = atoms to form a (substituted) 5-8 membered ring; R6 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl, aryl, heteroaryl; dotted line = optional double bond; with provisos], were prepared Thus, N-[2-(dimethylamino)ethyl]pyridine-2,3-diamine (preparation given) was heated with carbonyldiimidazole in DMF for 24 h at 75-80° to give 3-(2-dimethylaminoethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. This in THF was treated with 3-fluorophenylsulfonyl chloride, diisopropylamine, and DMAP followed by stirring for 12 h to give 3-(2-dimethylaminoethyl)-1-[(3-fluorophenyl)sulfonyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. I bound to serotonin 5-HT6 receptors with Ki = 4-80 nM.

L25 ANSWER 4 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:78225 HCAPLUS
DOCUMENT NUMBER: 142:176840
TITLE: Preparation of arylsulfonyldihydrobenzimidazolones as serotonin 5-HT6 receptor ligands.
INVENTOR(S): Cole, Derek Cecil; **Bernotas, Ronald Charles**
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005020575	A1	20050127	US 2004-897153	20040722
WO 2005009996	A1	20050203	WO 2004-US23243	20040719

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-489417P P 20030723
OTHER SOURCE(S): MARPAT 142:176840
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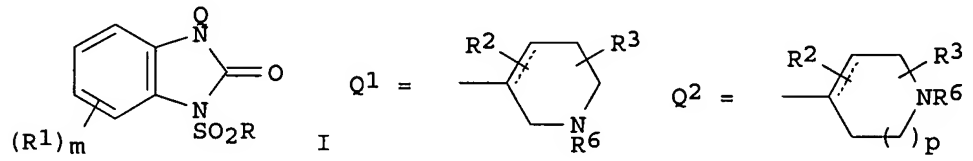


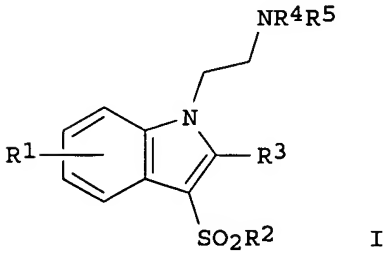
AB Title compds. [I; R = (substituted) alkyl, cycloalkyl, naphthyl, heteroaryl, N-bridgehead bicyclyl, tricyclyl; R1 = halo, cyano, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, etc.; m = 0-3; n = 2-5; p = 0-2; R2, R3 = H, (substituted) alkyl; R4, R5 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl, aryl, heteroaryl; R6 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl; Q = (CR2R3)nNR4R5, Q1, Q2; dotted line = optional double bond], were prepared Thus, 1-[2-(dimethylamino)ethyl]-1,3-dihydrobenzimidazol-2-one (preparation given) in THF was treated with 5-chlorothien-2-ylsulfonyl chloride, diisopropylethylamine, and dimethylaminopyridine followed by stirring for 16 h to give 1-[(5-chlorothien-2-yl)sulfonyl]-3-[2-(dimethylamino)ethyl]-1,3-dihydro-2H-benzimidazol-2-one. The latter bound to serotonin 5-HT6 receptors with Ki = 43 nM.

L25 ANSWER 5 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:48564 HCAPLUS
DOCUMENT NUMBER: 142:211413
TITLE: Discovery of 5-Arylsulfonamido-3- (pyrrolidin-2-ylmethyl)-1H-indole Derivatives as Potent, Selective 5-HT6 Receptor Agonists and Antagonists
AUTHOR(S): Cole, Derek C.; Lennox, William J.; Lombardi, Sabrina; Ellingboe, John W.; **Bernotas, Ronald C.**; Tawa, Gregory J.; Mazandarani, Hossein; Smith, Deborah L.; Zhang, Guoming; Coupet, Joseph; Schechter, Lee E.
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Pearl River, NY, 10965, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(2), 353-356
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal

LANGUAGE: English
AB 5-Arylsulfonylamido-3-(pyrrolidin-2-ylmethyl)-1H-indoles have been identified as high-affinity 5-HT6 receptor ligands. Within this class, several of the (R)-enantiomers were potent agonists having EC50 values of 1 nM or less and functioning as full agonists while the (S)-enantiomers displayed moderate antagonist activity.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1062658 HCAPLUS
TITLE: A short, novel approach to 2,3,4a,5-tetrahydro-1H-pyrazino[1,2-a]quinoline-4,6-diones. [Erratum to document cited in CA142:038216]
AUTHOR(S): **Bernotas, Ronald C.**
CORPORATE SOURCE: Aventis Pharmaceuticals, Bridgewater, NJ, 08807, USA
SOURCE: Synlett (2004), (14), 2646
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; Errata
LANGUAGE: English
AB An erratum.

L25 ANSWER 7 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:863092 HCAPLUS
DOCUMENT NUMBER: 142:56116
TITLE: 1-(2-Aminoethyl)-3-(arylsulfonyl)-1H-indoles as novel 5-HT6 receptor ligands
AUTHOR(S): **Bernotas, Ronald**; Lenicek, Steven; Antane, Schuyler; Zhang, Guo Ming; Smith, Deborah; Coupet, Joseph; Harrison, Boyd; Schechter, Lee E.
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Collegeville, PA, 19426, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(22), 5499-5502
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:56116
GI



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AB Novel 1-(2-aminoethyl)-3-(arylsulfonyl)-1H-indoles I [R1 = H, 5-F, 6-Cl, 6-MeO, 6-CN, 7-MeO, etc.; R2 = Ph, 4-MeC6H4, 3-FC6H4, 2-F3COC6H4, 1-naphthyl, PhCH2; R3 = H, Me; R4,R5 = H, Me; R4R5 = (CH2)5] were prepared Binding assays indicated these compds. are 5-HT6 receptor ligands, among which I (R1 = R3 = H; R2 = 1-naphthyl; R4 = R5 = Me) and I (R1 = R3 = R4 =

H; R2 = 1-naphthyl; R5 = Me) showed high affinity for 5-HT6 receptors with Ki = 3.7 and 5.7 nM, resp.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 8 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:858032 HCAPLUS
DOCUMENT NUMBER: 142:38216
TITLE: A short, novel approach to 2,3,4a,5-tetrahydro-1H-pyrazino[1,2-a]quinoline-4,6-diones
AUTHOR(S): **Bernotas, Ronald C.**
CORPORATE SOURCE: Aventis Pharmaceuticals, Bridgewater, NJ, 08807, USA
SOURCE: Synlett (2004), (12), 2165-2166
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:38216
AB An expeditious route to constrained arylpiperazinones has been developed. The key reaction formed the tricyclic system in one-pot via a 1,4-addition-lactamization-aromatic substitution sequence. Four examples were prepared
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:703120 HCAPLUS
DOCUMENT NUMBER: 141:207232
TITLE: Preparation of heterocyclyl-3-sulfonylindazoles as 5-hydroxytryptamine-6 ligands
INVENTOR(S): **Bernotas, Ronald Charles**; Yan, Yinfa; Robichaud, Albert Jean; Liu, Guangcheng
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 31 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004167122	A1	20040826	US 2004-778427	20040213
WO 2004074243	A2	20040902	WO 2004-US3926	20040210
WO 2004074243	A3	20041202		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-447613P P 20030214
OTHER SOURCE(S): MARPAT 141:207232
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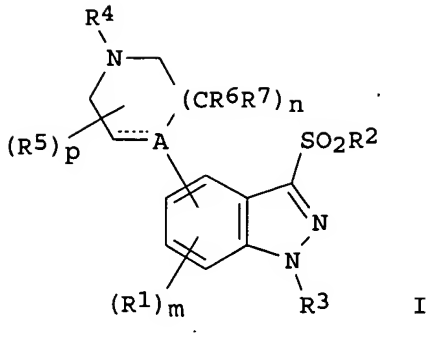

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AB The title compds. (I) [A = C, CR8, N; R1 = H, halogen, cyano, COR9, OCO2R10, CO2R11, CONR12R13, SOxR14, NR15R16, OR17, each (un)substituted C1-6 alkyl, C3-7 cycloalkyl, aryl, or heteroaryl; R2 = (un)substituted C1-6 alkyl, C3-7 cycloalkyl, aryl, heteroaryl group, (un)substituted 8- to 13-membered bicyclic or tricyclic ring having a N atom at the bridgehead and optionally containing 1, 2 or 3 addnl. heteroatoms selected from N, O or S; R3 = H, each (un)substituted C1-6 alkyl, C3-7 cycloalkyl, aryl, or heteroaryl; R4 = H, each (un)substituted C1-6 alkyl or C3-7 cycloalkyl; R5-R7 = H, each (un)substituted C1-6 alkyl or C3-7 cycloalkyl; m, p = an integer of 1-3; n = 1,2; R8 = H, OH, (un)substituted C1-6 alkoxy; R9, R10, R11, R17 = H, each (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-6 cycloalkyl, cycloheteroalkyl, aryl, or heteroaryl; R12, R13, R15, R16 = H or (un)substituted C1-4 alkyl or NR12R13 or NR15R16 together forms a 5- to 7-membered ring optionally containing another heteroatom selected from O, (un)substituted NH or SOx; R14 = each (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-6 cycloalkyl, cycloheteroalkyl, aryl, or heteroaryl; x = 0, 1, 2; the solid line with a dotted line represents a single bond or a double bond] or stereoisomers thereof or pharmaceutically acceptable salts thereof are prepared These compds. are modulators 5-HT6 receptor and useful in the therapeutic treatment of disorders related to or affected by the 5-HT6 receptor including motor disorder, anxiety disorder, cognitive disorder, neurodegenerative disorder, attention deficit disorder, obsessive compulsive disorder, withdrawal from drug, alc. or nicotine addiction, schizophrenia, depression, and Alzheimer's disease, stroke, head trauma, and neuropathic pain. For example, 5-(4-benzylpiperazin-1-yl)-1-(4-fluorophenyl)-3-phenylsulfonyl-1H-indazole hydrochloride at 1 μM inhibited by 74% the binding of [3H]-LSD to human cloned 5-HT6 receptor.

L25 ANSWER 10 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:701785 HCAPLUS
DOCUMENT NUMBER: 141:200209
TITLE: Heterocyclyl-3-sulfonylazaindole or-azaindazole derivatives as 5-HT6 receptor ligands, and their use for the treatment of central nervous system disorders
INVENTOR(S): **Bernotas, Ronald Charles**; Yan, Yinfa
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004167030	A1	20040826	US 2004-778441	20040213
WO 2004074286	A1	20040902	WO 2004-US3930	20040210

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-447515P P 20030214
OTHER SOURCE(S): MARPAT 141:200209

AB The invention provides the title compds. and their use for the treatment of a central nervous system disorder related to or affected by the 5-HT6 receptor. Preparation of e.g. 5-(4-methylpiperazin-1-yl)-3-(phenylsulfonyl)-1H-pyrazolo[4,3-b]pyridine hydrochloride is described.

L25 ANSWER 11 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:574514 HCAPLUS
DOCUMENT NUMBER: 141:260330
TITLE: Chloromethyl sulfones from sulfonyl chlorides via a one-pot procedure
AUTHOR(S): Antane, Schuyler; **Bernotas, Ronald**; Li, Yanfang; McDevitt, Robert; Yan, Yinfa
CORPORATE SOURCE: Wyeth Research, Chemical and Screening Sciences, Princeton, NJ, 08543-8000, USA
SOURCE: Synthetic Communications (2004), 34(13), 2443-2449
CODEN: SYNCAV; ISSN: 0039-7911
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:260330

AB A simplified one-pot transformation of a diverse set of aryl- and heteroaryl-sulfonyl chlorides into the corresponding chloromethyl sulfones is described.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 12 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:80697 HCAPLUS
DOCUMENT NUMBER: 140:146118
TITLE: Preparation of heterocyclylalkyl-sulfonylazaindole or -azaindazole derivatives 5-hydroxytryptamine-6 (5-HT6) ligands
INVENTOR(S): **Bernotas, Ronald Charles**; Lenicek, Steven Edward; Elokdah, Hassan Mahmoud; Li, David Zenan
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009600	A1	20040129	WO 2003-US22506	20030717
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2491251	AA	20040129	CA 2003-2491251	20030717
US 2004023970	A1	20040205	US 2003-621432	20030717
PRIORITY APPLN. INFO.:			US 2002-396949P P	20020718
			WO 2003-US22506 W	20030717

OTHER SOURCE(S): MARPAT 140:146118

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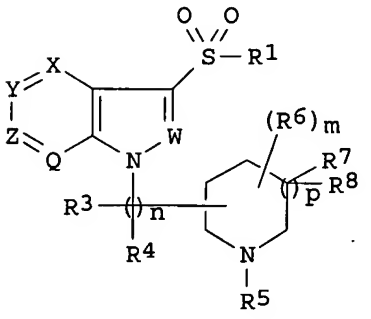

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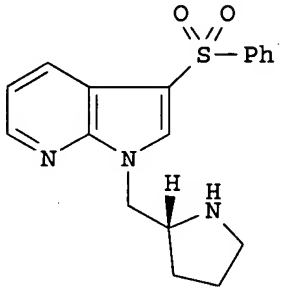


II

AB Title compds. I [W, X, Y, Z, Q = N, substituted C; R1 = (cyclo)alkyl, (hetero)aryl, etc.; R2 = H, halo, alkyl, alkoxy, etc.; R3-4 = H, alkyl; R5 = H, alk(en/yn)yl, etc.; R6 = alk(en/yn)yl, cycloalkyl, etc.; R7-8 = H, alk(en/yn)yl, cycloalkyl, etc.; m, n = 0-3; p = 0-2] are prepared For instance, 3-(Phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine (preparation given) is reacted with tert-Bu (2R)-2-[[[(4-methylphenyl)sulfonyl]oxy]methyl]-1-pyrrolidinecarboxylate (i. DMF, NaH, 0°; ii. dioxane, HCl, 4 h) to give II•HCl. II has Ki = 12 nM for the 5-HT6 receptor. I are useful for treatment of a central nervous system disorder related to or affected by the 5-HT6 receptor.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 13 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:80650 HCAPLUS

DOCUMENT NUMBER: 140:146005

TITLE: Preparation of 1-heterocyclylalkyl-3-sulfonylindoles and indazoles as 5-HT6 ligands

INVENTOR(S): **Bernotas, Ronald Charles**; Lenicek, Steven Edward

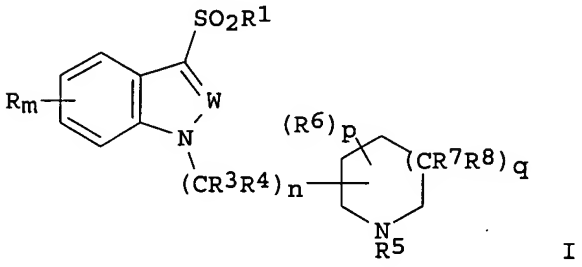
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004009548	A1	20040129	WO 2003-US22485		20030717
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2491248	AA	20040129	CA 2003-2491248		20030717
US 2004024023	A1	20040205	US 2003-621698		20030717
PRIORITY APPLN. INFO.:			US 2002-396958P	P	20020718
			WO 2003-US22485	W	20030717

OTHER SOURCE(S): MARPAT 140:146005
GI



I

AB Title compds. [I; W = N, CR2; R = halo, cyano, OCO2R9, CO2R10, CONR11R12, SOxR13, NR14R15, OR16, COR17, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl; R1 = (substituted) alkyl, cycloalkyl, aryl, heteroaryl, etc.; R2 = H, halo, (substituted) alkyl, alkoxy, cycloalkyl, aryl, heteroaryl; R3, R4 = H, (substituted) alkyl; R5 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl, aryl, heteroaryl; R6 = (substituted) alkyl, cycloalkyl, alkenyl, alkynyl; R7, R8 = H, (substituted) alkyl, cycloalkyl, alkenyl, alkynyl; m, n, p = 0-3; q, x = 0-2; R9, R10, R13, R17 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl, aryl, heteroaryl; R11, R12, R14, R15 = H, (substituted) alkyl; NR11R12, NR14R15 = 5-7 membered ring; R16 = (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl, aryl, heteroaryl; R18 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl, aryl, heteroaryl], were prepared Thus, 3-(phenylsulfonyl)-1H-indole (preparation given) in DMF at 0° was treated with sodium hydride in mineral oil stirred for 2 h at ambient temperature, treated with 4-(toluene-4-sulfonyloxymethyl)piperidine-1-carboxylic acid tert-Bu ester and the mixture was stirred for 16 h at 55° to

give tert-Bu 4-[3-(phenylsulfonyl)-1H-indol-1-ylmethyl]piperidine-1-carboxylate. The latter was stirred with 4N HCl in dioxane to give 82% 3-(phenylsulfonyl)-1-(piperidin-4-ylmethyl)-1H-indole hydrochloride, which showed 5-HT6 binding with Ki = 27 nM.

L25 ANSWER 14 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:972076 HCAPLUS
DOCUMENT NUMBER: 140:27761
TITLE: 1-(Aminoalkyl)-3-sulfonylazaindoles as 5-hydroxytryptamine-6 ligands
INVENTOR(S): **Bernotas, Ronald Charles**; Lenicek, Steven Edward; Antane, Schuyler A.
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003101990	A1	20031211	WO 2003-US17466	20030603
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003236278	A1	20031225	US 2003-453010	20030603
US 6825212	B2	20041130		
BR 2003011591	A	20050301	BR 2003-11591	20030603
EP 1509522	A1	20050302	EP 2003-734366	20030603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005085481	A1	20050421	US 2004-963132	20041012

PRIORITY APPLN. INFO.:		
US 2002-385502P	P	20020604
US 2003-453010	A3	20030603
WO 2003-US17466	W	20030603

OTHER SOURCE(S): MARPAT 140:27761
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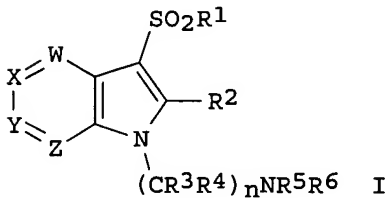


I

AB The present invention provides title compds. I (W, X, Y, Z = N or substituted C; n = 2-5; R1 = C1-C6 alkyl, C3-C7 cycloalkyl, aryl etc.; R2 = H, halogen, or a C1-C6 alkyl, C1-C6 alkoxy etc.; R3, R4 = H or C1-C6

alkyl group; R5, R6 = H or C1-C6 alkyl group, C2-C6 alkenyl etc.), and the use thereof for the therapeutic treatment of disorders relating to or affected by the 5-HT6 receptor. Thus, title compound I (R1 = 1-naphthyl; R2 = H; Z = N; X, Y, W = C; CR3R4 = CH2CH2; R5 = R6 = Me) was prepared (mp 203-206°) and demonstrated binding to the 5-hydroxytryptamine-6 receptor with Ki value 1 nM compared to 6.0 nM for clozapine.

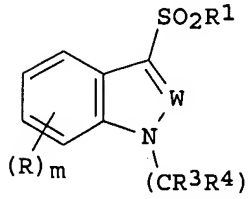
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 15 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:972055 HCAPLUS
DOCUMENT NUMBER: 140:27760
TITLE: 1-(Aminoalkyl)-3-sulfonylindole and -indazole derivatives as 5-hydroxytryptamine-6 ligands
INVENTOR(S): **Bernotas, Ronald Charles**; Lenicek, Steven Edward; Antane, Schuyler A.; Zhou, Ping; Li, Yanfang
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003101962	A1	20031211	WO 2003-US17472	20030603
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003232828	A1	20031218	US 2003-453009	20030603
US 6727246	B2	20040427		
EP 1509501	A1	20050302	EP 2003-736818	20030603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003011436	A	20050322	BR 2003-11436	20030603

PRIORITY APPLN. INFO.: US 2002-385695P P 20020604
WO 2003-US17472 W 20030603

OTHER SOURCE(S): MARPAT 140:27760
GI



I

AB The present invention relates to the preparation of aminoalkyl indole and

indazole I (W = N or substituted C; m = 1-3; n = 2-5; R = H, halogen, CN, C1-C6alkyl, C2-C6 alkenyl etc.; R1 = C1-C6 alkyl, C3-C7 cycloalkyl, aryl etc.; R2 = H, halogen, or a C1-C6 alkyl, C1-C6 alkoxy etc.; R3, R4 = H or C1-C6 alkyl group; R5, R6 = H or C1-C6 alkyl group, C2-C6 alkenyl etc.), and the use thereof for the treatment of central nervous system disorders related to or affected by the 5-HT6 receptor. Thus, (Rm = H, R1 = 1-naphthyl, R2 = H, n = 2, R5 = R6 = CH3) (mp 239-241°) prepared by reacting corresponding indole derivative with N,N-dimethyl-2-chloroethylamine showed 5-HT6 binding Ki of 4 nM compared to 6.0 nM for clozapine.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:634752 HCAPLUS
TITLE: Novel, potent 5HT2A antagonists
AUTHOR(S): Harris, Keith J.; Palermo, Mark; Knight, Julie; Shimshock, Steven; Bordeau, Kenneth J.; Fink, David M.; Kosley, Raymond; Wolf, Veronica; Chiang, Yulin; Lee, George; Rauckman, Barbara S.; **Bernotas, Ronald**; Sing, Lily; Hitchcock, Janice; Sorensen, Stephen; Kongsamut, Sam; Roehr, Joachim E.; Senyah, Yaw; Kominos, Dorothea
CORPORATE SOURCE: Chemistry, Aventis, Bridgewater, NJ, 07039, USA
SOURCE: Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), MEDI-144. American Chemical Society: Washington, D. C.
CODEN: 69EKY9
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB The synthesis and biol. evaluation of novel, potent 5HT2A antagonists will be described. These 1-heterocyclic-3-substituted piperazine compds. (1) exhibit potent 5HT2A binding in vitro. Several compds. were tested for in vivo 5HT2A antagonism (DMT mouse head twitch). Compound (2) below possessed oral activity in the DMT head twitch model.

L25 ANSWER 17 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:511332 HCAPLUS
DOCUMENT NUMBER: 139:85327
TITLE: Preparation of azaindolylalkylamines as 5-hydroxytryptamine-6 ligands
INVENTOR(S): **Bernotas, Ronald Charles**; Cole, Derek Cecil; Lennox, William Joseph
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053970	A1	20030703	WO 2002-US40220	20021217

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP 1456206	A1	20040915	EP 2002-795890		20021217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR 2002015151	A	20041019	BR 2002-15151		20021217
US 2003171395	A1	20030911	US 2002-323263		20021219
US 6800640	B2	20041005			
US 2005020598	A1	20050127	US 2004-922678		20040819
PRIORITY APPLN. INFO.:			US 2001-342838P	P	20011220
			WO 2002-US40220	W	20021217
			US 2002-323263	A1	20021219

OTHER SOURCE(S): MARPAT 139:85327

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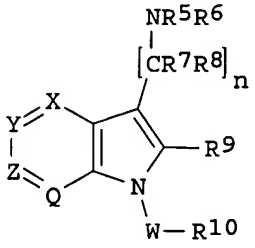


I

AB The title compds. [I; W = SO2, CO, CONR11, CSNR12; X = N, CR1; Y = N, CR2; Z = N, CR3; Q = N, CR4, with the proviso that no more than two of X, Y, Z and Q may be N; n = 2-3; R1-R4 = H, halo, CN, etc.; R5, R6 = H, alkyl, cycloalkyl, etc.; R7, R8 = H, (un)substituted alkyl; R9 = H, halo, alkyl, etc.; R10 = (un)substituted alkyl, aryl, heteroaryl, etc.; R11, R12 = H, (un)substituted alkyl, aryl, heteroaryl], useful for the therapeutic treatment of disorders relating to or affected by the 5-HT6 receptor, were prepared E.g., a multi-step synthesis of I [X = N; Y, Z, Q = CH; W = SO2; R5-R9 = H; R10 = 2-ClC6H4; n = 2], starting with 2-chloro-3-nitropyridine and tert-Bu cyanoacetate, which showed Ki of 5.0 nM against 5-HT6 binding, was given.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 18 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:450102 HCAPLUS

TITLE: Parallel solution phase synthesis of N-arylsulfonyl indoles, -indazoles, and -azaindoles as 5-hydroxytryptamine-6-ligands

AUTHOR(S): Cole, Derek C.; Lennox, William J.; Stock, Joseph R.; Zhou, Ping; Ellingboe, John; **Bernotas, Ronald C.**; Smith, Deborah L.; Schechte, Lee E.; Zhang, Guoming

CORPORATE SOURCE: Wyeth Research, Pearl River, NY, USA

SOURCE: Abstracts, 31st Northeast Regional Meeting of the American Chemical Society, Saratoga Springs, NY, United States, June 15-18 (2003), 173. American Chemical Society: Washington, D. C.
CODEN: 69EBFV

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

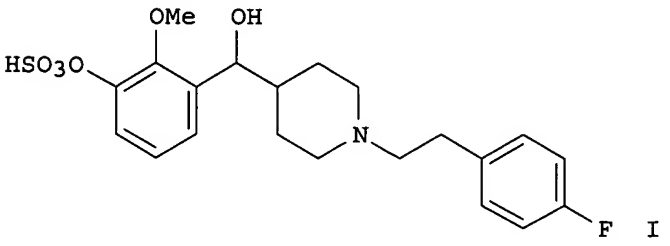
AB 5-Hydroxytryptamine-6 (5-HT6) has been cloned from rat cDNA based on its homol. to G-protein-coupled receptors. Rat and human 5-HT6 mRNA is found in the striatum, amygdala, nucleus accumbens, hippocampus, cortex and olfactory tubercle, but not found in the peripheral organs. Pharmacol. studies indicate that a variety of antipsychotic agents have high affinity for the 5-HT6 receptor suggesting a potential therapeutic target for the treatment of psychiatric diseases. Behavioral studies have implicated a role for 5-HT6 in cognition enhancement. We have investigated series of N-arylsulfonyl indoles, -indazoles, and -azaindoles as 5-HT6 ligands. The parallel library synthesis and biol. evaluation of these classes of compds. will be presented.

L25 ANSWER 19 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:790226 HCAPLUS
DOCUMENT NUMBER: 137:310813
TITLE: Preparation of sulfuric acid mono-[3[[1-[2-(4-fluorophenyl)ethyl]-piperidin-4-yl]hydroxymethyl]-2-methoxyphenyl]ester and enantiomers as 5HT2A antagonists.
INVENTOR(S): **Bernotas, Ronald Charles**; Brown, Paul Wayne; Emmons, Gary Thomas; King, Chi-hsin Richard
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA
SOURCE: U.S., 19 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6465490	B1	20021015	US 2000-615246	20000713
US 2003087932	A1	20030508	US 2002-200821	20020722
US 6716986	B2	20040406		
US 2004152900	A1	20040805	US 2004-760515	20040120

PRIORITY APPLN. INFO.:
US 1999-198215P P 19990716
US 2000-615246 A3 20000713
US 2002-200821 A3 20020722

OTHER SOURCE(S): CASREACT 137:310813
GI



AB Title compds. I were prepared Thus, acetic acid [1-[2-(4-fluorophenyl)ethyl]piperidin-4-yl](3-hydroxy-2-methoxyphenyl)methyl ester (preparation given) was heated at 45° with SO3.pyridine in MeCN for 18

h; H2O, MeOH, and K2CO3 were added followed by 12 h reflux to give sulfuric acid mono-(+)-[3[[1-[2-(4-fluorophenyl)ethyl]piperidin-4-yl]hydroxymethyl]-2-methoxyphenyl] ester. Title compds. were shown to penetrate the blood-brain barrier.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 20 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:63973 HCAPLUS
DOCUMENT NUMBER: 134:115860
TITLE: Preparation of sulfuric acid mono-[3-({1-[2-(4-fluoro-phenyl)-ethyl]-piperidin-4-yl}-hydroxy-methyl)-2-methoxy-phenyl]ester and analogs for use as serotonin 5HT2A receptor antagonists
INVENTOR(S): **Bernotas, Ronald**; Brown, Paul; Emmons, Gary; King, Chi-Hsin
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005764	A2	20010125	WO 2000-US19065	20000713
WO 2001005764	A3	20011004		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2374635	AA	20010125	CA 2000-2374635	20000713
BR 2000012477	A	20020402	BR 2000-12477	20000713
EP 1202967	A2	20020508	EP 2000-947304	20000713
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003505374	T2	20030212	JP 2001-511425	20000713
AU 769484	B2	20040129	AU 2000-60939	20000713
NZ 516286	A	20040326	NZ 2000-516286	20000713
ZA 2002000101	A	20030404	ZA 2002-101	20020104
NO 2002000213	A	20020222	NO 2002-213	20020115

PRIORITY APPLN. INFO.: US 1999-354704 A2 19990716
WO 2000-US19065 W 20000713

OTHER SOURCE(S): MARPAT 134:115860
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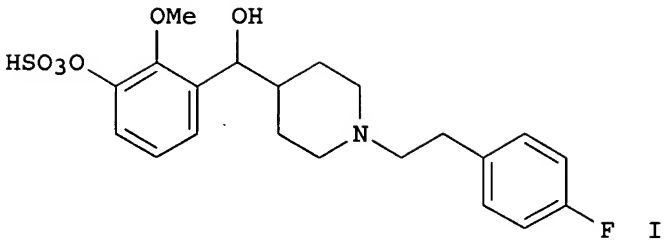

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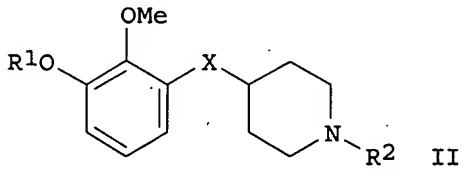


II

AB Preparation of the title compound I and its analogs II (R1 = H, trialkylsilane, alkylcarboxy; R2 = (un)substituted arylalkyl, COOR3, H; R3 = alkyl, aryl or arylalkyl; X = CO or CHOR4; R4 = H or alkylcarboxy) is disclosed. Thus, compound I was prepared by combined sulfonation/deacetylation of acetic acid {1-[2-(4-fluorophenyl)-ethyl]-piperidin-4-yl}-(3-hydroxy-2-methoxyphenyl)methyl ester. I is an active metabolite of II (R1 = Me; X = CHOH; R2 = 4-FC6H4CH2CH2) and a method for its preparation and isolation via metabolism is claimed. The title compds. are claimed as serotonin 5HT2A receptor antagonists and as such are useful for the treatment of a number of disease states, e.g. schizophrenia, anxiety, variant angina, anorexia nervosa, cardiac arrhythmias, etc.

L25 ANSWER 21 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:300316 HCAPLUS
DOCUMENT NUMBER: 131:19267
TITLE: [3+2] cycloaddition reactions of proline benzyl ester nitrone with alkenes and alkynes
AUTHOR(S): **Bernotas, Ronald C.**; Sabol, Jeffrey S.; Sing, Lily; Friedrich, Dirk
CORPORATE SOURCE: Hoechst Marion Roussel, Inc., Bridgewater, NJ, 08807, USA
SOURCE: Synlett (1999), (5), 653-655
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:19267
AB 1,2-Didehydroproline benzyl ester N-oxide was synthesized. It readily underwent [3+2] cycloaddns. with a variety of alkenes and alkynes to give isoxazolidines and isoxazolines, resp., with good to excellent regio- and diastereoselectivity.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 22 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:86846 HCAPLUS
DOCUMENT NUMBER: 126:195016
TITLE: Evidence for a novel pentyl radical adduct of the

cyclic nitrone spin trap MDL 101,002
AUTHOR(S): Dage, Jeffrey L.; Ackermann, Bradley L.; Barbuch, Robert J.; **Bernotas, Ronald C.**; Ohlweiler, David F.; Haegele, Klaus D.; Thomas, Craig E.
CORPORATE SOURCE: Hoechst Marion Roussel, Inc., Cincinnati, OH, USA
SOURCE: Free Radical Biology & Medicine (1997), 22(5), 807-812
CODEN: FRBMEH; ISSN: 0891-5849
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 3,4-Dihydro-3,3-dimethyl-isoquinoline-2-oxide (MDL 101,002) is a conformationally constrained cyclic analog of the known spin trap α-Ph N-tert-Bu nitrone (PBN). Because of PBN's ability to scavenge free radicals, MDL 101,002 is currently being evaluated in stroke models as a means to ameliorate the oxidative insult associated with reperfusion injury. To augment our understanding of the radical scavenging mechanism of this potential drug, MDL 101,002 was incubated with soybean lipoxygenase in the presence of linoleic acid to study the interaction between MDL 101,002 and free radicals formed during lipid peroxidn. Anal. of the reaction mixture was performed by high performance liquid chromatog. using normal phase conditions with detection by atmospheric pressure chemical ionization mass spectrometry (APCI-MS). Similar to the work by Iwahashi et al. [Arch. Biochem. Biophys., 1991, 285, 172], who studied the spin trap α-(4-pyridyl-1-oxide)-N-tert-Bu nitrone (4-POBN), an adduct that suggested the trapping of pentyl radicals by MDL 101,002 was observed However, the apparent mol. ion for this adduct (246 Da) was 1 Da lower than would be predicted if a pentyl radical had simply added to MDL 101,002. In addition, the adduct exhibited significant absorbance at 304 nm, consistent with the unsatd. nitrone structure of MDL 101,002. To account for these observations, it is postulated that, after the initial capture of a pentyl radical, subsequent abstraction of a hydrogen atom by a neighboring radical occurs to regenerate a nitrone (1-pentyl analog of MDL 101,002). We present evidence for this adduct and offer a mechanism for its formation. These findings indicate that mass spectroscopic anal. of stable nitrone radical adducts may be useful in the identification of radical-dependent damage in vivo and possibly in clin. development of MDL 101,002 as an antioxidant pharmaceutical.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 23 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:632485 HCAPLUS
DOCUMENT NUMBER: 125:328663
TITLE: 2,3,4,4a,5,6-Hexahydro-1H-pyrazino[1,2-a]quinoline synthesis via a [3+2] cycloaddition
AUTHOR(S): **Bernotas, Ronald C.**; Adams, Ginette
CORPORATE SOURCE: Hoechst Marion Roussel, Inc., Cincinnati, OH, 45215, USA
SOURCE: Tetrahedron Letters (1996), 37(41), 7343-7344
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 125:328663
AB A constrained aryl piperazine, 2,3,4,4a,5,6-hexahydro-1H-pyrazino[1,2-a]quinoline, has been synthesized using an intramol. aromatic substitution as the key step.

L25 ANSWER 24 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:632484 HCAPLUS

DOCUMENT NUMBER: 125:328662
TITLE: Synthesis of a 1-benzylpiperazin-2-one nitrone and its reaction with alkynes and alkenes
AUTHOR(S): **Bernotas, Ronald C.**; Adams, Ginette
CORPORATE SOURCE: Hoechst Marion Roussel, Inc., Cincinnati, OH, 45215, USA
SOURCE: Tetrahedron Letters (1996), 37(41), 7339-7342
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 125:328662
AB 1-Benzylpiperazin-2-one nitrone (I) was prepared in 3 steps from 4-(tert-butoxycarbonyl)piperazin-2-one. I readily undergoes [3+2] cycloaddns. with alkynes and alkenes to give Δ4-isoxazolines and isoxazolidines, resp., which can be reductively opened to 3-substituted piperazin-2-ones and 1,3-amino alcs.

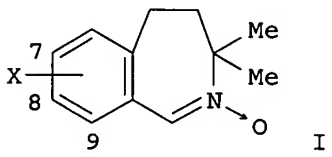
L25 ANSWER 25 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:525627 HCAPLUS
DOCUMENT NUMBER: 125:247579
TITLE: Thermal cleavage of oxazolidine-4,5-diones to imines: a short synthesis of 3,4-dihydro-3,3-dimethyl-7-trifluoromethylisoquinoline 2-oxide
AUTHOR(S): **Bernotas, Ronald C.**; Adams, Ginette; Nieduzak, Thaddeus R.
CORPORATE SOURCE: Hoechst Marion Roussel, Cincinnati, OH, 45215, USA
SOURCE: Synthetic Communications (1996), 26(18), 3471-3477
CODEN: SYNCAV; ISSN: 0039-7911
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of oxazolidine-4,5-diones was thermally cleaved to cyclic imines in excellent yield. This reaction was utilized in an efficient synthesis of 3,4-dihydroisoquinoline-based nitrone.

L25 ANSWER 26 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:389705 HCAPLUS
DOCUMENT NUMBER: 125:104874
TITLE: In vitro and in vivo activity of a novel series of radical trapping agents in model systems of CNS oxidative damage
AUTHOR(S): Thomas, Craig E.; Carney, John M.; **Bernotas, Ronald C.**; Hay, David A.; Carr, Albert A.
CORPORATE SOURCE: Marion Merrell Dow Research Institute, Cincinnati, OH, 45215-6300, USA
SOURCE: Annals of the New York Academy of Sciences (1994), 738(Neurobiology of NO• and •OH), 243-249
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many laboratory and clin. studies have suggested that oxygen radical formation and resultant cell damage contribute to CNS injury following stroke and neurotrauma. Therefore, antioxidants represent a viable therapeutic approach for management of CNS oxidative damage. The spin trap α-phenyl-tert-Bu nitrone (PBN) has recently been shown to protect against stroke-induce damage and reduce aging-associated neurol. deficits. A cyclic analog of PBN, MDL 101,002, was prepared and tested in a number of in vitro and in vivo assays designed to assess its neuroprotective

properties. MDL 101,002 was found to be an effective •OH trap, to inhibit lipid peroxidn., and to decrease infarct size in a gerbil model of stroke. These results further indicate that oxidative damage arising from stroke contributes to infarct formation, and that spin traps are effective in ameliorating ischemia and reperfusion-induced CNS injury.

L25 ANSWER 27 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:344478 HCAPLUS
DOCUMENT NUMBER: 125:114441
TITLE: Synthesis and radical scavenging activity of 3,3-dialkyl-3,4-dihydroisoquinoline 2-oxides
AUTHOR(S): **Bernotas, Ronald C.**; Thomas, Craig E.; Carr, Albert A.; Nieduzak, Thaddeus R.; Adams, Ginette; Ohlweiler, David F.; Hay, David A.
CORPORATE SOURCE: Hoechst Marion Roussel, Cincinnati, OH, 45215, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(10), 1105-1110
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The synthesis and antioxidant activities of several cyclic nitrones related to Ph t-Bu nitrone (PBN) are described. These nitrones may act as radical scavengers and have potential uses in the treatment of stroke and septic shock.

L25 ANSWER 28 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:294182 HCAPLUS
DOCUMENT NUMBER: 125:58295
TITLE: Synthesis of benzazepine-based nitrones as radical traps
AUTHOR(S): **Bernotas, Ronald C.**; Adams, Ginette; Carr, Albert A.
CORPORATE SOURCE: Hoechst Marion Roussel, Cincinnati, OH, 45215, USA
SOURCE: Tetrahedron (1996), 52(19), 6519-6526
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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AB Benzazepine-based nitrones were synthesized utilizing a modified Bischler-Napieralski reaction as the key step. These compds. are cyclic analogs of the radical trap Ph tert-Bu nitrone. The target compds. were the 4,5-dihydro-3,3-dimethyl-3H-2-benzazepine 2-oxides I (X = H, 8-chloro, 7,9-dichloro).

L25 ANSWER 29 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:101994 HCAPLUS
DOCUMENT NUMBER: 124:219400
TITLE: Characterization of the radical trapping activity of a

novel series of cyclic nitrone spin traps
AUTHOR(S): Thomas, Craig E.; Ohlweiler, David F.; Carr, Albert A.; Nieduzak, Thaddeus R.; Hay, David A.; Adams, Ginette; Vaz, Roy; **BErnotas, Ronald C.**
CORPORATE SOURCE: Hoechst Marion Roussel, Inc., Cincinnati, OH, 45215, USA
SOURCE: Journal of Biological Chemistry (1996), 271(6), 3097-104
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB α-Phenyl-tert-Bu nitrone (PBN) is a nitrone spin trap, which has shown efficacy in animal models of oxidative stress, including stroke, aging, sepsis, and myocardial ischemia/reperfusion injury. We have prepared a series of novel cyclic variants of PBN and evaluated them for radical trapping activity in vitro. Specifically, their ability to inhibit iron-induced lipid peroxidn. in liposomes was assessed, as well as superoxide anion (O2) and hydroxyl radical (.OH) trapping activity as determined biochem. and using ESR (ESR) spectroscopy. All cyclic nitrones tested were much more potent as inhibitors of lipid peroxidn. than was PBN. The unsubstituted cyclic variant MDL 101,002 was approx. 8-fold more potent than PBN. An anal. of the analogs of MDL 101,002 revealed a direct correlation of activity with lipophilicity. However, lipophilicity does not solely account for the difference between MDL 101,002 and PBN, inasmuch as the calculated octanol/water partition coefficient for MDL 101,002 is 1.01 as compared to 1.23 for PBN. This indicated the cyclic nitrones are inherently more effective radical traps than PBN in a membrane system. The most active compound was a dichloro analog in the seven-membered ring series (MDL 104,342), which had an IC50 of 26 μM, which was 550-fold better than that of PBN. The cyclic nitrones were shown to trap .OH with MDL 101,002 being 20-25 times more active than PBN as assessed using 2-deoxyribose and p-nitrosodimethylaniline as substrates, resp. Trapping of .OH by MDL 101,002 was also examined by using ESR spectroscopy. When Fenton's reagent was used, the .OH adduct of MDL 101,002 yielded a six-line spectrum with hyperfine coupling consts. distinct from that of PBN. Importantly, the half-life of the adduct was nearly 5 min, while that of PBN is less than 1 min at physiol. pH. MDL 101,002 also trapped the O2 radical to yield a six-line spectrum with coupling consts. very distinct from that of the .OH adduct. In mice, the cyclic nitrones ameliorated the damaging effects of oxidative stress induced by ferrous iron injection into brain tissue. Similar protection was not afforded by the lipid peroxidn. inhibitor U74006F, thus implicating radical trapping as a unique feature in the prevention of cell injury. Together, the in vivo activity, the stability of the nitroxide adducts, and the ability to distinguish between trapping of .OH and O2 suggest the cyclic nitrones to be ideal reagents for the study of oxidative cell injury.

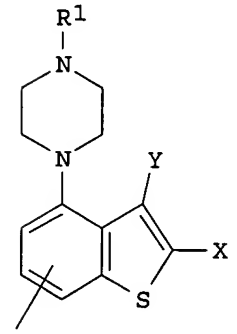
L25 ANSWER 30 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:761964 HCAPLUS
DOCUMENT NUMBER: 123:286094
TITLE: 4-Piperazinylbenzo[b]thiophene derivatives as serotonin receptor agents
INVENTOR(S): **Bernotas, Ronald C.**; Sprouse, Jeffrey S.; Cheng, Hsien C.
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals Inc., USA
SOURCE: U.S., 35 pp. Cont.-in-part of U.S. Ser. No. 79,692, abandoned.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5436246	A	19950725	US 1993-119791	19930915
WO 9406789	A1	19940331	WO 1993-US8865	19930917
W: AU, CA, FI, HU, JP, KR, NO, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 660832	A1	19950705	EP 1993-922253	19930917
EP 660832	B1	19890114		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08501559	T2	19960220	JP 1994-508371	19930917
JP 3298107	B2	20020702		
HU 72662	A2	19960528	HU 1995-796	19930917
AU 671494	B2	19960829	AU 1993-51321	19930917
AU 9351321	A1	19940412		
AT 162190	E	19980115	AT 1993-922253	19930917
ES 2112434	T3	19980401	ES 1993-922253	19930917
CA 2144947	C	20000201	CA 1993-2144947	19930917
FI 9501249	A	19950316	FI 1995-1249	19950316
NO 9501015	A	19950515	NO 1995-1015	19950316
NO 310461	B1	20010709		

PRIORITY APPLN. INFO.:
US 1992-947007 B1 19920917
US 1993-79692 B2 19930617
US 1993-119791 A 19930915
WO 1993-US8865 W 19930917

OTHER SOURCE(S): MARPAT 123:286094
GI



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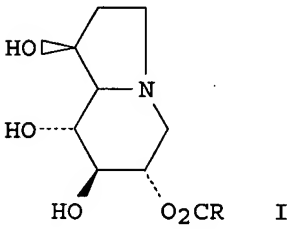
AB A method is claimed for producing an agonist effect at the 5HT1A or 5HT1D receptor comprising administering title compound I in which Y is represented by hydrogen or C1-3 alkyl; R is represented by a substituent selected from the group consisting of hydrogen, C1-4 alkyl, C1-4 alkoxy, halogen, CF3, OCF3, and OH; R1 is represented by hydrogen, cycloalkyl, C1-6 alkyl, Ph optionally substituted, phenylalkyl, or phenylamidoalkyl; X is represented by hydrogen, (CH2)nX1, CH:CHX1 or CHX2(CH2)qCH3 ; n is an integer from 0-2; q is either the integer 0 or 1; X1 is represented by OH, OR2, NR2R3, CO2R2, CONR2R3, CN, or COR2; R2 and R3 are each independently represented by hydrogen, C1-4 alkyl, Ph optionally substituted, phenylalkyl, or R2 and

R3 together form a (CH2)m cycloalkyl, where m=2-6; X2 is OR4 or NR4R5 in which R4 and R5 are each independently hydrogen or C1-4 alkyl; and the pharmaceutically acceptable addition salts thereof; with the proviso that when n is 0 or X is CH:CHX1, then X1 is not OH, OR2, or NR2R3; to a patient in need thereof. Thus, e.g, treatment of Et 4-[4-(2-phenylethyl)-1-piperazinyl]benzo[b]thiophene-2-carboxylate (preparation given) with LiAlH4 afforded 4-[4-(2-phenylethyl)-1-piperazinyl]benzo[b]thiophene-2-methanol monohydrochloride which demonstrated IC50 =0.6(2) nM (5HT1A binding affinity) and IC50 =2.4(2) nM (5HT1D binding affinity).

L25 ANSWER 31 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:421209 HCAPLUS
DOCUMENT NUMBER: 123:228698
TITLE: Castanospermine analogs: their inhibition of glycoprotein processing α-glucosidases from porcine kidney and B16F10 cells
AUTHOR(S): Kang, Mohinder S.; Liu, Paul S.; **Bernotas, Ronald C.**; Harry, Brenda S.; Sunkara, Prasad S.
CORPORATE SOURCE: Marion Merrell Dow Inc., Cincinnati, OH, 45215, USA
SOURCE: Glycobiology (1995), 5(1), 147-52
CODEN: GLYCE3; ISSN: 0959-6658
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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AB We have used a simple and efficient procedure for the synthesis of N-5-carboxypentyl-1-deoxynojirimycin, an affinity ligand for α-glucosidase I (Bernotas, R. C. and Ganem, B., Biochem. J., 270, 539-540, 1990). The affinity gel was used to purify α-glucosidase I in one step from crude extract In subsequent steps, partially purified α-glucosidase II was obtained. We have synthesized several castanospermine analogs, e.g. I [R = (CH2)nMe, Me2CHNH, cyclopropyl, 2-furyl, Ph, NHPh, Bn, n = 2-4, 6, 8, 14], of and studied their inhibition of α-glucosidase I in vitro using purified α-glucosidase I and in vivo in cultured B16F10 cells. Although the castanospermine analogs were significantly less active against the purified enzyme (IC50 .apprx.1-23 μg/mL) as compared to castanospermine (IC50 = 0.02 μg/mL), several compds. had up to 30-fold higher activity than castanospermine against α-glucosidase I in B16F10 cells, based on the accumulation of G3M7-9N2 oligosaccharide-containing glycoproteins. These results suggest that these analogs with lipophilic side chains cross the membrane barrier more efficiently than castanospermine. Once inside the cell, they may be converted to their active metabolite, castanospermine, by cellular esterases to give enzyme inhibition.

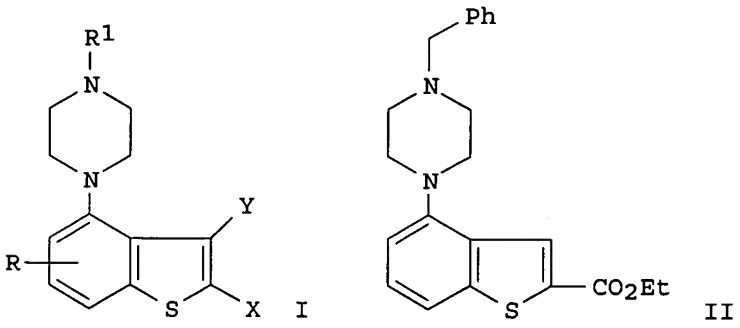
L25 ANSWER 32 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:266954 HCAPLUS

DOCUMENT NUMBER: 122:56053
TITLE: 4-(piperazinyl)benzothiophenes as serotonin receptor agents
INVENTOR(S): **Bernotas, Ronald C.**; Sprouse, Jeffrey S.; Cheng, Hsien C.
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9406789	A1	19940331	WO 1993-US8865	19930917
W: AU, CA, FI, HU, JP, KR, NO, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5436246	A	19950725	US 1993-119791	19930915
EP 660832	A1	19950705	EP 1993-922253	19930917
EP 660832	B1	19890114		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08501559	T2	19960220	JP 1994-508371	19930917
JP 3298107	B2	20020702		
AU 671494	B2	19960829	AU 1993-51321	19930917
AU 9351321	A1	19940412		
CA 2144947	C	20000201	CA 1993-2144947	19930917
NO 9501015	A	19950515	NO 1995-1015	19950316
NO 310461	B1	20010709		

PRIORITY APPLN. INFO.:
US 1992-947007 A 19920917
US 1993-79692 A 19930617
US 1993-119791 A 19930915
WO 1993-US8865 W 19930917

OTHER SOURCE(S): MARPAT 122:56053
GI



AB The present invention discloses substituted 4-(piperazinyl)benzothiophenes I (R = H, alkyl, etc.; R1 = H, alkyl, cycloalkyl, etc.; X = H, alkyl, alkenyl, etc.; Y = H, alkyl) that are serotonin 5HT1A and 5HT1D receptor agonists. I are antidepressants or anxiolytics. An example compound, Et 4-[4-(phenylmethyl)-1-piperazinyl]benzo[b]thiophene-2-carboxylate (II) showed affinity toward 5-HT1A receptors (IC50 >1000 nM).

L25 ANSWER 33 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:409168 HCAPLUS

DOCUMENT NUMBER: 121:9168
TITLE: Preparation of cyclic nitrones, and their use in treating shock
INVENTOR(S): Carr, Albert A.; Thomas, Craig E.; **Bernotas, Ronald C.**; Ku, George
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals Inc., USA
SOURCE: U.S., 20 pp. Cont.-in-part of U.S. Ser. No. 828,075, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5292746	A	19940308	US 1992-926109	19920805
ZA 9206781	A	19930401	ZA 1992-6781	19920907
CA 2077708	AA	19930313	CA 1992-2077708	19920908
CA 2077708	C	20030805		
AU 9222800	A1	19930318	AU 1992-22800	19920908
AU 652662	B2	19940901		
IL 103111	A1	19960723	IL 1992-103111	19920908
KR 232025	B1	19991201	KR 1992-16533	19920909
NO 9203538	A	19930315	NO 1992-3538	19920911
NO 179514	B	19960715		
NO 179514	C	19961023		
EP 532027	A1	19930317	EP 1992-115575	19920911
EP 532027	B1	20000712		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 05213870	A2	19930824	JP 1992-267790	19920911
JP 3255989	B2	20020212		
HU 67022	A2	19950130	HU 1992-2923	19920911
HU 216788	B	19990830		
FI 101071	B1	19980415	FI 1992-4076	19920911
AT 194599	E	20000715	AT 1992-115575	19920911
PT 532027	T	20001031	PT 1992-115575	19920911
ES 2149161	T3	20001101	ES 1992-115575	19920911
US 5397789	A	19950314	US 1993-170543	19931220
US 5498778	A	19960312	US 1994-352470	19941209
US 5525615	A	19960611	US 1995-458314	19950602
US 5527812	A	19960618	US 1995-458318	19950602
US 5532252	A	19960702	US 1995-458311	19950602
US 5677315	A	19971014	US 1995-458310	19950602
GR 3034551	T3	20010131	GR 2000-402241	20001004

PRIORITY APPLN. INFO.:
US 1991-758063 B2 19910912
US 1992-828075 B2 19920130
US 1992-926109 A 19920805
US 1993-170543 A3 19931220
US 1994-352470 A3 19941209

OTHER SOURCE(S): MARPAT 121:9168
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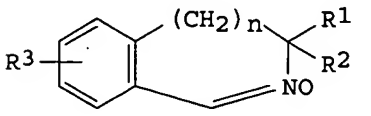

I

AB Title compds. I (R1, R2 = C1-3 alkyl, R1R2 = C2-7 alkylene; R3 = H, halo, C1-4 alkyl, C1-4 alkoxy, F3C, F3CO, HO; n = 0-2), spin trapping agents, useful as inhibitors of interleukin-1 secretion and for treatment of shock, are prepared To 1-benzyl-1-formamidocyclohexane was added (COCl)2 to give after workup spiro[cyclohexane-1,3']-3,4-dihydroisoquinoline which was treated with H2O2 to give I (R1-3 = H, n = 1) (II). In endotoxin-treated rats, II at 10 mg/kg showed 91% survival.

L25 ANSWER 34 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:472506 HCAPLUS
DOCUMENT NUMBER: 119:72506
TITLE: Preparation of cyclic nitrones as spin trapping agents.
INVENTOR(S): Carr, Albert Anthony; Thomas, Craig Eugene; **Bernotas, Ronald Charles**; Ku, George
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals, Inc., USA
SOURCE: Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 532027	A1	19930317	EP 1992-115575		19920911
EP 532027	B1	20000712			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
US 5292746	A	19940308	US 1992-926109		19920805
ZA 9206781	A	19930401	ZA 1992-6781		19920907
PRIORITY APPLN. INFO.:			US 1991-758063	A	19910912
			US 1992-828075	A	19920130
			US 1992-926109		19920805

OTHER SOURCE(S): MARPAT 119:72506
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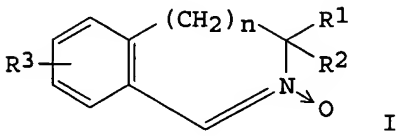


I

AB Title compds. I (R1, R2 = C1-3 alkyl, R1R2 = C2-7 alkylene; R3 = H, halo, C1-4 alkyl,C1-4 alkoxy, F3c, F3CO, HO; n = 0-2) useful for spin trapping for therapeutic oxygen radical scavenging and as interleukin-1 inhibitors, are prepared To PhCH2CM2NHCHO in MePh was added P2O5, the mixture refluxes for 6 h, allowed to stand overnight at room temperature, and basified with 50% NaOH to give 3,4-dihydro-3,3-dimethylisoquinoline to which in CH2Cl2 was added 3-ClC6H4COO2H to give 4,8b-dihydro-3,3-dimethyl-3H-oxazirino[3,2a]isoquinoline to which in MeOH and H2O was added H2SO4 to give I (R1 = R2 = Me, R = H) (II). In endotoxin-treated rats after 72 h exposure, II at 30 mg/kg showed 83% survival.

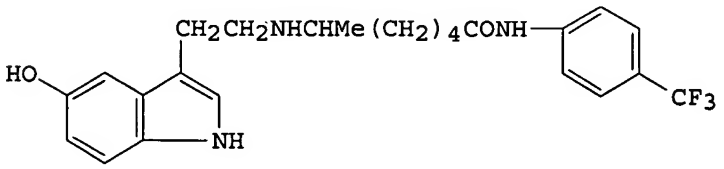
L25 ANSWER 35 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:490136 HCAPLUS
DOCUMENT NUMBER: 117:90136
TITLE: Preparation of N-phenyl-ω-[(heterocyclylalkyl)amino]alkanamides as serotoninergic agonists
INVENTOR(S): McDonald, Ian A.; Dudley, Mark W.; **Bernotas, Ronald C.**; Sprouse, Jeffrey S.
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals Inc., USA
SOURCE: Eur. Pat. Appl., 35 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 478954	A1	19920408	EP 1991-114456	19910828
EP 478954	B1	20001018		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5189179	A	19930223	US 1991-735700	19910730
CA 2049803	AA	19920301	CA 1991-2049803	19910823
AU 9182664	A1	19920305	AU 1991-82664	19910823
AU 641535	B2	19930923		
ZA 9106710	A	19920527	ZA 1991-6710	19910823
IL 99306	A1	19950330	IL 1991-99306	19910826
FI 9104065	A	19920301	FI 1991-4065	19910828
NO 9103384	A	19920302	NO 1991-3384	19910828
NO 175430	B	19940704		
NO 175430	C	19941012		
HU 59092	A2	19920428	HU 1991-2810	19910828
AT 197040	E	20001115	AT 1991-114456	19910828
ES 2153346	T3	20010301	ES 1991-114456	19910828
CN 1059717	A	19920325	CN 1991-108614	19910829
CN 1030766	B	19960124		
JP 04270264	A2	19920925	JP 1991-242328	19910829
US 5387604	A	19950207	US 1992-962434	19921016
US 5559143	A	19960924	US 1994-319916	19941007
GR 3035062	T3	20010330	GR 2000-402750	20001213

PRIORITY APPLN. INFO.: US 1990-574710 A 19900829
US 1991-735700 A 19910730
US 1992-962434 A3 19921016

OTHER SOURCE(S): MARPAT 117:90136
GI



I

AB RBN(X)CHYZ1DCON(Z)R1 [B-alkylene; D = bond, alkylene; R = (substituted) 3-indolyl, -2,3-dihydro-1,4-benzodioxin-2-yl; R1 = (substituted) Ph; X, Y, Z = H, alkyl, (substituted) Ph; Z1 = (substituted) alkylene] were prepared as serotoninergic S1A and S1D agonists (no data). Thus, serotonin was reductively condensed with MeCO(CH2)4CONHC6H4(CF3)-4 to give title compound

I.

L25 ANSWER 36 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:207641 HCAPLUS
DOCUMENT NUMBER: 114:207641
TITLE: The use of triphenylphosphine-diethyl azodicarboxylate (DEAD) for the cyclization of 1,4- and 1,5-amino alcohols
AUTHOR(S): **Bernotas, Ronald C.**; Cube, Rowena V.
CORPORATE SOURCE: Merrell Dow Res. Inst., Cincinnati, OH, 45215, USA
SOURCE: Tetrahedron Letters (1991), 32(2), 161-4
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:207641
AB Application of the Mitsunobu reagent (Ph3P/di-Et azodicarboxylate) to the cyclization of 1,4- and 1,5-amino alcs. provided an assortment of azacycles in good to excellent yield.

L25 ANSWER 37 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:112317 HCAPLUS
DOCUMENT NUMBER: 114:112317
TITLE: Synthesis and properties of ferroelectric 4-[4-(S-1-methylheptyloxy)benzoyloxy]-4'-alkyloxycarbonylbiphenyls
AUTHOR(S): Adomeniene, O.; Adomenas, P.; **Bernotas, R.**; Petraitis, J.; Jakubeniene, M.
CORPORATE SOURCE: Vilnius Univ., Vilnius, USSR
SOURCE: Molecular Crystals and Liquid Crystals (1990), 191, 187-91
CODEN: MCLCA5; ISSN: 0026-8941
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Synthesis, mesomorphic properties and spontaneous polarization values of 4-[4-(S-1-methyl-heptyloxy)benzoyloxy]-4'-alkyloxycarbonylbiphenyls are given.

L25 ANSWER 38 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:77437 HCAPLUS
DOCUMENT NUMBER: 114:77437
TITLE: Easy assembly of ligands for glycosidase affinity chromatography
AUTHOR(S): **Bernotas, Ronald C.**; Ganem, Bruce
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Biochemical Journal (1990), 270(2), 539-40
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An improved, high-yield synthesis of the corresponding N-carboxypentyl derivs. of 3 iminoalditol glycosidase inhibitors has been developed for affinity chromatog. enzyme purification Reductive amination of 1-deoxynojirimycin (or its D-manno or D-galacto analogs) with methyl 5-formylvalerate and NaBH3CN at neutral pH afforded an aminoester which upon hydrolysis with aqueous 5% HCl gave the desired amino acid in 97% overall yield. These amino acids could then be covalently attached using water-soluble carbodiimide to 6-aminohexyl Sepharose 4B.

L25 ANSWER 39 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:41713 HCAPLUS
DOCUMENT NUMBER: 114:41713

TITLE: Enzymatic preparation of the enantiomers of some 1-phenyl-1-alkanols
AUTHOR(S): Mori, Kenji; **Bernotas, Rokas**
CORPORATE SOURCE: Dep. Agric. Chem., Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Tetrahedron: Asymmetry (1990), 1(2), 87-96
CODEN: TASYE3; ISSN: 0957-4166
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:41713

AB The acetates of racemic 1-phenyl-1-heptanol, 1-phenyl-1-octanol, and 1-phenyl-1-nonanol were hydrolyzed by Pseudomonas lipase in 10% acetone-0.1 M phosphate buffer (pH 6.9) at 30°. Due to remarkable differences in the rates of hydrolysis of the enantiomeric acetates, the reaction led to (R)-(+)-alcs. (92.2-97.8% e.e.) and (S)-(-)-acetates (99.6-100.0% e.e.). Slow reverse esterification of 1-phenyl-1-octnaol took place in the presence of 1 equivalent of acetic acid. Addition of Et acetate markedly increased the rate of esterification to give (R)-(+)-1-phenyloctyl acetate (92.8% e.e.). Attempts to esterify racemic alcs. in organic solvents were unsuccessful because of low reaction rate and/or low enantioselectivity.

L25 ANSWER 40 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:631865 HCAPLUS
DOCUMENT NUMBER: 113:231865
TITLE: A new family of five-carbon iminoalditols which are potent glycosidase inhibitors
AUTHOR(S): **Bernotas, Ronald C.**; Papandreou, George; Urbach, Jonathan; Ganem, Bruce
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, 14853, Norway
SOURCE: Tetrahedron Letters (1990), 31(24), 3393-6
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:231865
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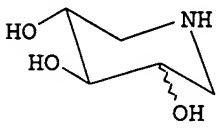

I

AB The preparation of iminoalditols, e.g. I, from Me 6-bromo-6-deoxy-α-D-glucopyranoside is described. I inhibited the same group of enzymes, e.g., β-glucosidase and α-mannosidase.

L25 ANSWER 41 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:552210 HCAPLUS
DOCUMENT NUMBER: 113:152210
TITLE: The use of Pearlman's catalyst for selective N-debenzylation in the presence of benzyl ethers
AUTHOR(S): **Bernotas, Ronald C.**; Cube, Rowena V.
CORPORATE SOURCE: Merrell Dow Res. Inst., Cincinnati, OH, 45215, USA
SOURCE: Synthetic Communications (1990), 20(8), 1209-12
CODEN: SYNCAV; ISSN: 0039-7911
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:152210

AB Hydrogenation with 20% palladium hydroxide on carbon selectively removes benzyl groups from amines in high yields without cleaving benzyl ethers.

L25 ANSWER 42 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:515733 HCAPLUS
DOCUMENT NUMBER: 113:115733
TITLE: A short, versatile approach to polyhydroxylated pyrrolidines utilizing a reductive elimination-reductive amination as a key step
AUTHOR(S): **Bernotas, Ronald C.**
CORPORATE SOURCE: Merrell Dow Res. Inst., Cincinnati, OH, 45215, USA
SOURCE: Tetrahedron Letters (1990), 31(4), 469-72
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:115733
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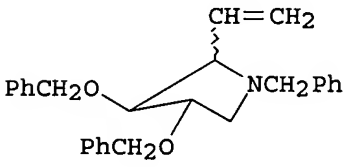

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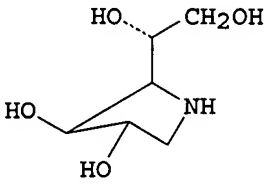

II

AB An efficient synthesis of epimeric pyrrolidines I starting from Me 4,6-O-benzylidene gluco- and galactopyranosides gave ready access to hydroxylated pyrrolidines, e.g., II.

L25 ANSWER 43 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:75940 HCAPLUS
DOCUMENT NUMBER: 110:75940
TITLE: A new class of endoglycosidase inhibitors. Studies on endocellulases
AUTHOR(S): Liotta, Louis J.; **Bernotas, Ronald C.**; Wilson, David B.; Ganem, Bruce
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Journal of the American Chemical Society (1989), 111(2), 783-5
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:75940
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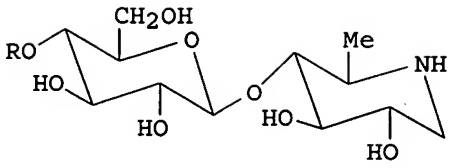

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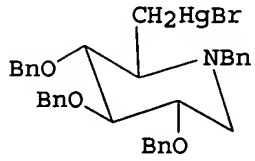

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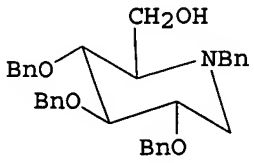
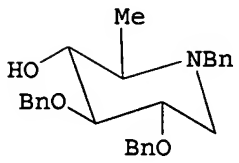


V



VI

AB Oligosaccharide analogs I [R = H, β-1,4-glucopyranosyl (II), β-1,4-cellobiosyl (III)] were synthesized by an unusual radical rearrangement. Reductive oxygenation of organomercurial IV (Bn = PhCH2) to alc. V also produced VI resulting from C4-benzyl ether removal and concomitant reduction at C6. Changing the flow of oxidant from a vigorous flux of pure O2 to a slow stream of air (0.04 mL/s) improved the yield of VI to 68%. The scope of this reaction was probed with several other mercurials. II and III competitively inhibited three (E1, E2 and E5) of the five β-1,4-endocellulases isolated from the cellulolytic bacterium Thermomonospora fusca.

L25 ANSWER 44 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:423268 HCAPLUS
DOCUMENT NUMBER: 109:23268
TITLE: Synthesis of (+)-1,5-dideoxy-1,5-imino-D-galactitol, a potent α-D-galactosidase inhibitor
AUTHOR(S): **Bernotas, Ronald C.**; Pezzone, Michael A.; Ganem, Bruce
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Carbohydrate Research (1987), 167, 305-11
CODEN: CRBRAT; ISSN: 0008-6215
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 109:23268
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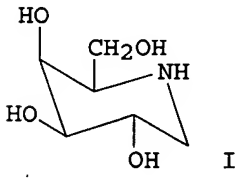

I

AB The title compound (I) was prepared as its hydrochloride from Me α-D-galactopyranoside. I is a potent α-D-galactosidase inhibitor and causes elevation of total kidney-glucolipid and ceramide trihexoside levels in mice.

L25 ANSWER 45 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:2541 HCAPLUS

DOCUMENT NUMBER: 108:2541
TITLE: (3R,4R,5S)-5-acetamido-3,4-piperidinediol: a selective hexosaminidase inhibitor
AUTHOR(S): **Bernotas, Ronald C.**; Ganem, Bruce
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Carbohydrate Research (1987), 167, 312-16
CODEN: CRBRAT; ISSN: 0008-6215
DOCUMENT TYPE: Journal
LANGUAGE: English
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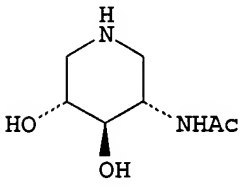

I

AB Me 2-acetamido 3,4-di-O-benzyl-2-deoxy-D-glucopyranoside prepared as a mixture of anomers was coverted to 6-bromo derivative mixts. by treatment with mesyl chloride-Et3N and then LiBr-2-butanone. Reductive ring cleavage with activated Zn, PhCH2NH2, and NaBH3CN in PrOH-H2O (9:1) followed by in situ reductive amination, subsequently ozonolysis with reductive workup, reductive amination and debenzylation with Pd-C, EtOH and HCl, gave I. Bovine β-hexosaminidase was 50% inhibited by I at 0.1mM, whereas almond β-D-glucosidase, bovine β-D-galactosidase, endoglycosidase F and H were unaffected at 1.0mM.

L25 ANSWER 46 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:29253 HCAPLUS
DOCUMENT NUMBER: 106:29253
TITLE: Design and synthesis of sugar-specific glycosidase inhibitors
AUTHOR(S): **Bernotas, Ronald Charles**
CORPORATE SOURCE: Cornell Univ., Ithaca, NY, USA
SOURCE: (1986) 143 pp. Avail.: Univ. Microfilms Int., Order No. DA8607290
From: Diss. Abstr. Int. B 1986, 47(2), 628
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L25 ANSWER 47 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:424547 HCAPLUS
DOCUMENT NUMBER: 105:24547
TITLE: Synthesis of 2S-carboxy-3R,4R,5S-trihydroxypiperidine, a naturally occurring inhibitor of β-D-glucuronidase
AUTHOR(S): **Bernotas, Ronald C.**; Ganem, Bruce
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Tetrahedron Letters (1985), 26(41), 4981-2
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 105:24547
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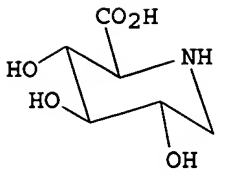

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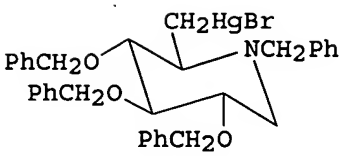

II

AB The glucuronic acid analog I of 1-deoxynojirimycin was synthesized in good overall yield from bromomercurial II by stepwise oxidation and debenzylation.

L25 ANSWER 48 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:523832 HCAPLUS
DOCUMENT NUMBER: 103:123832
TITLE: Efficient preparation of enantiomerically pure cyclic aminoalditols, total synthesis of 1-deoxynojirimycin and 1-deoxymannojirimycin
AUTHOR(S): **Bernotas, Ronald C.**; Ganem, Bruce
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Tetrahedron Letters (1985), 26(9), 1123-6
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 103:123832
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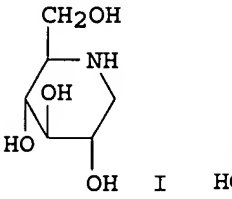

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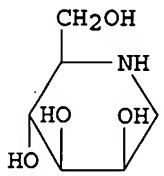

II

AB The title compds. (I and II) were prepared by methods involving a high-yield, ring-forming aminomercuration. I was obtained in several steps from Me α-D-glucopyranoside in 35% overall yield. II was obtained in several steps from Me α-D-mannopyranoside in 13% overall yield.

L25 ANSWER 49 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:192129 HCAPLUS
DOCUMENT NUMBER: 100:192129
TITLE: Total syntheses of (+)-castanospermine and (+)-deoxynojirimycin
AUTHOR(S): **Bernotas, Ronald C.**; Ganem, Bruce
CORPORATE SOURCE: Baker Lab., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Tetrahedron Letters (1984), 25(2), 165-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
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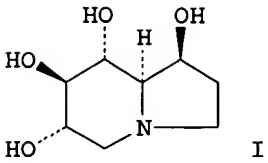

I

AB The absolute configuration of castanospermine (I) was determined by total synthesis
from D-glucose.

L25 ANSWER 50 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:603478 HCAPLUS
DOCUMENT NUMBER: 95:203478
TITLE: Chiral nematic tolans
AUTHOR(S): **Bernotas, R.**; Adomenas, P.
CORPORATE SOURCE: Chem. Dep., V. Kapsukas Vilnius Univ., Vilnius, 232006, USSR
SOURCE: Adv. Liq. Cryst. Res. Appl., Proc. Liq. Cryst. Conf. Soc. Countries, 3rd (1981), Meeting Date 1979, Volume 2, 1019-22. Editor(s): Bata, Lajos. Pergamon: Oxford, Engl.
CODEN: 46KUA2
DOCUMENT TYPE: Conference
LANGUAGE: English
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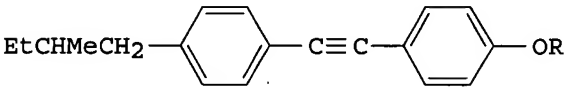

I

AB Liquid crystals I (R = Me, Et, Pr, Bu, pentyl, hexyl, heptyl, decyl) were synthesized and transition temps. and enthalpies of fusion were measured.

L25 ANSWER 51 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:524545 HCAPLUS
DOCUMENT NUMBER: 95:124545
TITLE: 4-[(+)-2-Methylbutyl]-4'-alkoxytolan possessing chiral nematic liquid crystal properties
INVENTOR(S): **Bernotas, R.**; Sirutkajtis, R.; Adomenas, P.
PATENT ASSIGNEE(S): Vilnius State University, USSR
SOURCE: U.S.S.R. From: Otkrytiya, Izobret., Prom. Obraztsy, Tovarnye Znaki 1981, (20), 257-8.
CODEN: URXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
SU 754815	A1	19810530	SU 1979-2713095	19790112
PRIORITY APPLN. INFO.:			SU 1979-2713095 A	19790112

AB (+)-p-EtCHMeCH2C6H4C.tplbond.CC6H4OR-p (R = C6H13, C7H15, C10H21) have chiral nematic properties.

L25 ANSWER 52 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1977:155484 HCAPLUS
DOCUMENT NUMBER: 86:155484
TITLE: Synthesis and some reactions of N-(β-acylethyl)aminopyridines and -aminoquinolines
AUTHOR(S): Denys, G.; Gureviciene, J.; Macionyte, V.; **Bernotas, R.**; Cekuoliene, L.
CORPORATE SOURCE: Vil'nyus. Gos. Univ. im. Kapsukasa, Vilnius, USSR
SOURCE: Zhurnal Organicheskoi Khimii (1977), 13(1), 199-204
CODEN: ZORKAE; ISSN: 0514-7492
DOCUMENT TYPE: Journal
LANGUAGE: Russian
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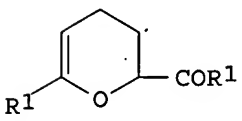

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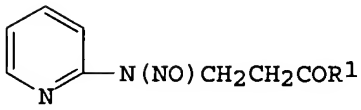

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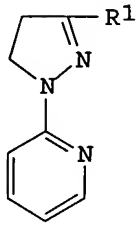

IV

AB Reaction of RNH2 (R = 2-, 3-, 4-pyridyl, 4-methyl-2-pyridyl, 2-, 3-, 4-, 5-, 6-, 8-quinolyl) with R1COCH2CH2NMe2 (R1 = Ph, p-MeOC6H4, p-BrC6H4, p-O2NC6H4, p-tolyl, p-ClC6H4) gave RNHCH2CH2COR1 (I), RN(CH2CH2COR1)2 and II. I (R1 = Ph, R = 5-, 6-, and 8-quinolyl) were cyclized by refluxing their HCl salts in PrOH. Reaction of I (R = 2-pyridyl, R1 = Ph, p-MeOC6H4) with HNO2 gave III, which were cyclized with Zn to give IV. Treatment of IV with S gave the resp. 1H-pyrazole.

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L25 52 SEA FILE=HCAPLUS ABB=ON PLU=ON ("BERNOTAS R"/AU OR "BERNOTAS ROKAS"/AU OR "BERNOTAS RONALD"/AU OR "BERNOTAS RONALD C"/AU OR "BERNOTAS RONALD CHARLES"/AU)
L26 3 SEA FILE=HCAPLUS ABB=ON PLU=ON ("LENICEK S"/AU OR "LENICEK STEVEN"/AU OR "LENICEK STEVEN EDWARD"/AU) NOT L25

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L26 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:120921 HCAPLUS
DOCUMENT NUMBER: 142:219150
TITLE: A preparation of 3-aminochroman and 2-aminotetralin derivatives, useful in the treatment of serotonin-mediated disorders
INVENTOR(S): Hatzenbuhler, Nicole Theriault; Evrard, Deborah Ann; Mewshaw, Richard Eric; Zhou, Dahui; Shah, Uresh Shantilal; Inghrim, Jennifer Ann; **Lenicek, Steven Edward**; Baudy, Reinhardt Bernhard; Butera, John Anthony; Sabb, Annmarie L.; Failli, Amedeo Arturo;

Ramamoorthy, Pudukkaraipudur Sivaramakrishnan
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 233 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005012291	A1	20050210	WO 2004-US24549		20040729
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2005032873	A1	20050210	US 2004-898866		20040726
PRIORITY APPLN. INFO.:			US 2003-491137P	P	20030730
			US 2003-491794P	P	20030801
			US 2004-898866	A	20040726

OTHER SOURCE(S): MARPAT 142:219150
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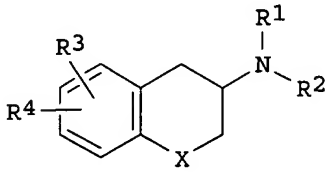

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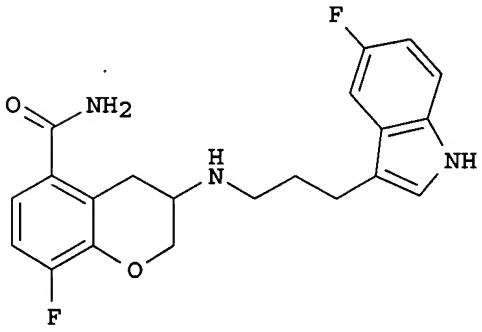

II

AB The invention relates to a preparation of 3-aminochroman and 2-aminotetralin derivs. of formula I [wherein: X is O or CH2; R1 is H, (cyclo)alkyl, or oxetane, etc.; R2 is (CH2)2-4-R5; R3 is OMe, C(O)(alkyl), or heterocycle, etc.; R4 is H or halogen; R5 is derivative of indole, benzothiophene, or benzofuran, etc.], useful in the treatment of serotonin-mediated disorders. The invention compds. are useful for the treatment of serotonin-mediated disorders such as depression and anxiety. For

instance, (indolylpropylamino)chroman derivative II (5-HT transporter affinity: Ki = 7 nM, 5-HT1A function cAMP: EC50 = 228.5 nM) was prepared via N-alkylation of 3-amino-8-fluorochroman-5-carboxamide by 3-(3-bromopropyl)-5-fluoro-1H-indole with a yield of 60%.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:282557 HCAPLUS
DOCUMENT NUMBER: 138:304162
TITLE: Preparation of 2-(aminoalkyl)chromans and benzofurans as 5-hydroxytryptamine-6 ligands for treatment of CNS disorders
INVENTOR(S): Kelly, Michael Gerard; Greenblatt, Lynne Padilla; Zhang, Gan; Palmer, Yvette Latko; **Lenicek, Steven Edward**
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003029239	A1	20030410	WO 2002-US31151	20020930
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003153599	A1	20030814	US 2002-263913	20021003
US 6638972	B2	20031028		
PRIORITY APPLN. INFO.:			US 2001-326970P P	20011004
OTHER SOURCE(S):	MARPAT 138:304162			

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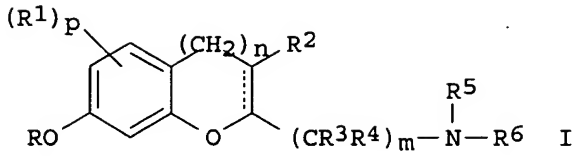

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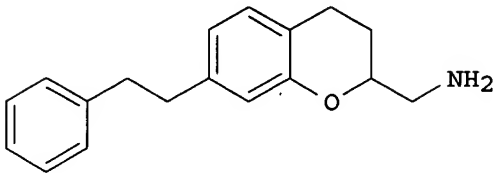

II

AB The present invention provides a compound I and the use thereof for the therapeutic treatment of disorders relating to or affected by the 5-HT6 receptor. Title compds. I [wherein R = (un)substituted alkyl or (hetero)aryl; R1 = halo, CN, OR7, CO2R8, CONR9R10, SOxR11, or (un)substituted alkyl, alkenyl, alkynyl, cyclo(hetero)alkyl, Ph, or heteroaryl; R2, R3, and R4 = independently H or (un)substituted alkyl; R5 and R6 = independently H or (un)substituted alkyl or (hetero)cycloalkyl; or NR5R6 = (un)substituted heterocyclyl; m = 1-4; n = 0-1; p = 0-3; x = 0-2; R7 = H, CO2R12, or (un)substituted alkyl, alkenyl, alkynyl, or (hetero)aryl; R8 and R12 = independently H or (un)substituted alkyl, alkenyl, alkynyl, cyclo(hetero)alkyl, or (hetero)aryl; R9 and R10 = independently H or (un)substituted alkyl; R11 = (un)substituted alkyl or (hetero)aryl; or stereoisomers or pharmaceutically acceptable salts thereof] were prepared as 5-hydroxytryptamine-6 (5-HT6) ligands. For example, cycloaddn. of 2',4'-dihydroxyacetophenone with di-Et oxalate in NaOEt and EtOH provided Et 7-hydroxy-4-oxo-4H-benzopyran-2-carboxylate (68%). Hydrogenation with Pd/C in AcOH to the chroman (96%), reaction of the alc. with benzyl chloride in the presence of K2CO3 and KI in acetone to the ether (100%), and reduction of the ester to the hydroxymethyl derivative (93%) gave [(7-benzyloxy)chroman-2-yl]methanol. Bromination (100%), amination using potassium phthalimide and NH2NH2•H2O in DMF, and conversion to the salt afforded II•HCl. The latter exhibited binding to the 5-HT6 receptor with Ki of 15 nM in cultured HeLa cells expressing human cloned 5-HT6 receptors. Thus, I are useful for the treatment of CNS disorders, such as motor disorder, anxiety, cognitive disorder, schizophrenia, depression, Alzheimer's disease, Parkinson's disease, and attention deficit disorder (no data).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:796115 HCAPLUS

TITLE: In vitro activity of chiral analogs of the serotonin 5-HT1A silent antagonist WAY-100635.

AUTHOR(S): **Lenicek, S.**; Kelly, M. G.; Childers, W. E.; Greenblatt, L.; Sabb, A.; Zhang, G.; Palmer, Y.; Podlesny, E.; Vogel, R.; Smith, D. L.; Schechter, L. E.

CORPORATE SOURCE: Chemical Sciences and Neuroscience, Wyeth-Ayerst Research, Princeton, NJ, 08543, USA

SOURCE: Abstracts of Papers, 220th ACS National Meeting,

Washington, DC, United States, August 20-24, 2000
(2000) MEDI-118
CODEN: 69FZC3
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
AB Silent antagonists at the 5-HT1A receptor, e.g. WAY-100635, are potential therapeutic agents for various CNS disorders. With the aim of improving pharmacol. properties, a series of chiral amino acid-derived compds. (1) was prepared, varying the substituent on the 1-position of the alkyl chain. The 5-HT1A in vitro binding and SAR of the compds. will be presented.

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L25 52 SEA FILE=HCAPLUS ABB=ON PLU=ON ("BERNOTAS R"/AU OR "BERNOTAS ROKAS"/AU OR "BERNOTAS RONALD"/AU OR "BERNOTAS RONALD C"/AU OR "BERNOTAS RONALD CHARLES"/AU)
L26 3 SEA FILE=HCAPLUS ABB=ON PLU=ON ("LENICEK S"/AU OR "LENICEK STEVEN"/AU OR "LENICEK STEVEN EDWARD"/AU) NOT L25
L27 57 SEA FILE=HCAPLUS ABB=ON PLU=ON ("ELOKDAH H"/AU OR "ELOKDAH HASSAN"/AU OR "ELOKDAH HASSAN M"/AU OR "ELOKDAH HASSAN MAHMOUD"/AU) NOT (L25 OR L26)

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L27 ANSWER 1 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:300437 HCAPLUS
DOCUMENT NUMBER: 142:355272
TITLE: A preparation of heteroarylbenzofuran derivatives, useful as PAI-1 inhibitors
INVENTOR(S): **Elokdah, Hassan Mahmoud**; McFarlane, Geraldine Ruth; Mayer, Scott Christian
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030760	A1	20050407	WO 2004-US31364	20040924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-506012P P 20030925
US 2004-947840 A 20040923

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of heteroarylbenzofuran derivs. of formula I [wherein: R, R1, R2, and R3 are independently selected from H, (cyclo)alkyl, alkanoyl, halogen, OH, aryl, or NH2, etc.; R4 is H, alk(en/yn)yl, aryl, arylalkenyl, or C(:S)-alkyl, etc.; R5 is H, alkyl, aryl, or arylalkyl; X1, X2, X3, X4, X5, X6, X7, and X8 are independently selected from C or N, wherein at least one of X1-X8 is a nitrogen atom; Y is (CH2)0-6; A is CO2H, acid mimic, or salt], useful as PAI-1 inhibitors. For instance, benzofuranyl(tetrazolylmethoxy)quinoline derivative II (20% inhibition at 25 μM) was prepared via heterocyclization of [(benzofuranylquinolinyl)oxy]acetonitrile derivative III with sodium azide with a yield of 73%.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:300393 HCAPLUS
DOCUMENT NUMBER: 142:355053
TITLE: Preparation of Biphenyloxycarboxylic acids and derivatives thereof as inhibitors of PAI-1
INVENTOR(S): Commons, Thomas Joseph; Croce, Susan Christman; Trybulski, Eugene John; **Elokdah, Hassan Mahmoud**; Crandall, David Leroy
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030702	A1	20050407	WO 2004-US31458	20040924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-505989P P 20030925
US 2004-947710 A 20040923

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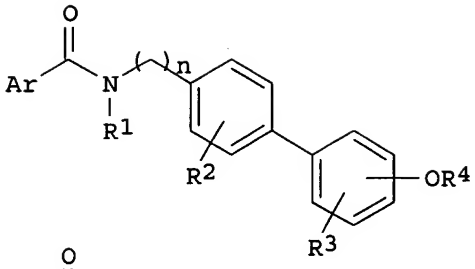

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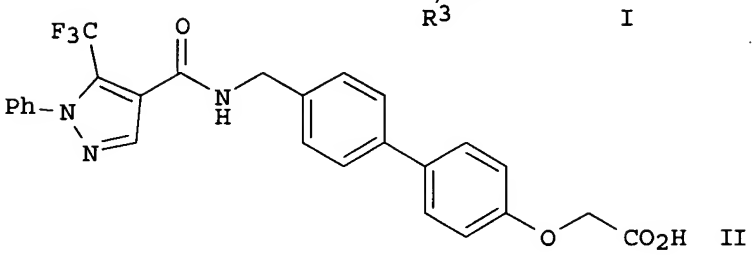

II

AB Title compds. I [Ar = Ph, naphthyl, furanyl, etc.; R1 = H, alkyl, alkylphenyl; R2-3 = H, alkyl, halo, etc.; R4 = alkylcarboxy, alkyltetrazole, etc.; n = 0-1] are prepared For instance, [[4'-[[[[1-phenyl-5-(trifluoromethyl)-1H-pyrazol-4-yl]carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]oxy]acetic acid (II) is prepared in 6 steps from 4'-Hydroxybiphenyl-4-carbonitrile, Me bromoacetate and 1-phenyl-5-trifluoromethyl-1H-pyrazole-4-carbonyl chloride. II exhibited 1% inhibition of PAI-1 at 25 μM and 60% inhibition at 100 μM. I are useful for the treatment of, e.g., thrombosis.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 3 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:300247 HCAPLUS
DOCUMENT NUMBER: 142:373672
TITLE: A preparation of benzofuran derivatives, useful as PAI-1 inhibitors
INVENTOR(S): Havran, Lisa Marie; Butera, John Anthony; **Elokdah, Hassan Mahmoud**; Jenkins, Douglas John; Gundersen, Eric Gould
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030199	A1	20050407	WO 2004-US31361	20040924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-505801P P 20030925
US 2004-947930 A 20040923

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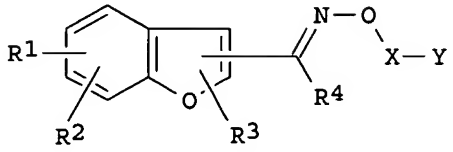

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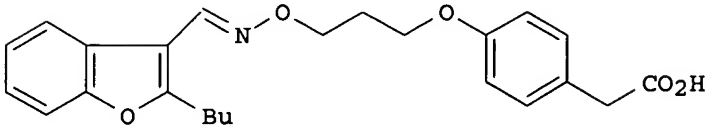

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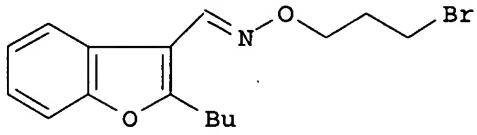

III

AB The invention relates to a preparation of benzofuran derivs. of formula I [wherein: R1 and R2 are independently selected from H, halogen, alkyl, OH, NH2, or (hetero)aryl, etc.; R3 is H, (cyclo)alkyl, heteroaryl, or CH2-cycloalkyl, etc.; R4 is H or (cyclo)alkyl; Y is 1-3 substituted Ph derivative; X is (cyclo)alkylene, (CH2)1-6-O, or (CH2)1-6-NH], useful as PAI-1 inhibitors. The invention compds. are useful for treatment of impairment of the fibrinolytic system, thrombosis, or cardiovascular diseases, etc. For instance, benzofuran derivative II (IC50 = 31.35 μM) was prepared via coupling of benzofurancarbaldehyde oxime derivative III with Me (4-hydroxyphenyl)acetate with a yield of 39%.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 4 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:300241 HCAPLUS
DOCUMENT NUMBER: 142:355162
TITLE: Preparation of 4-(1H-indol-3-yl-methylideneaminoxypropoxy)benzoic acid derivatives and related compounds as PAI-1 inhibitors for the treatment of impairment of the fibrinolytic system and of thrombosis
INVENTOR(S): Havran, Lisa Marie; Butera, John Anthony; **Elokdah, Hassan Mahmoud**; Jenkins, Douglas John; Gundersen, Eric Gould
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030192	A1	20050407	WO 2004-US31456	20040924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-505801P P 20030925
US 2004-947846 A 20040923

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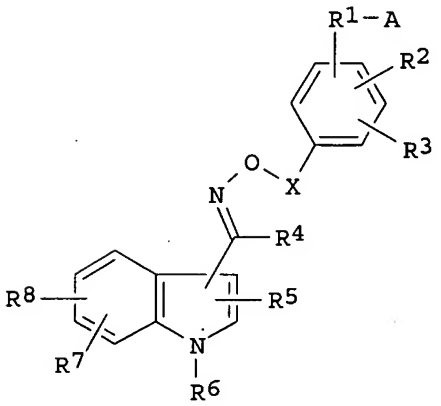

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AB Title compds. I [R1 = bond, alkylene, etc.; R2-3 = H, halo, alkyl, etc.; R4 = H, (cyclo)alkyl; A = COOH, carboxy mimic; X = alkylene, cycloalkylene; R5 = H, alkyl, cycloalkyl, etc.; R6 = H, (cyclo)alkyl, etc.; R7-8 = H, halo, alkyl, perfluoroalkyl, etc.] are prepared For instance, (E)-4-[3-[[[(1-Benzyl-1H-indol-3-yl)methylidene]amino]oxy]propoxy]-2-[(4-tert-butylbenzoyl)amino]benzoic acid (II) is prepared in 9 steps from 4-nitroanthranilic acid, 4-(tert-butyl)benzoyl chloride and 1-benzyl-1H-indol-3-carboxaldehyde O-(3-hydroxypropyl)oxime (preparation given). II has IC50 = 11.81 μM for PAI-1. I are useful for the treatment of fibrinolytic system thrombosis.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 5 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:284149 HCAPLUS
DOCUMENT NUMBER: 142:336368
TITLE: A preparation of naphthylbenzothiophene derivatives, useful as inhibitors of plasminogen activator inhibitor-1 (PAI-1)
INVENTOR(S): **Elokdah, Hassan Mahmoud**; McFarlane, Geraldine Ruth
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA

SOURCE: U.S. Pat. Appl. Publ., 25 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005070587	A1	20050331	US 2004-947898	20040923
WO 2005030750	A1	20050407	WO 2004-US31397	20040924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-505982P P 20030925
US 2004-947898 A 20040923

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of naphthylbenzothiophene derivs. of formula I [wherein: R1 and R3 are independently selected from H, (cyclo)alkyl, halogen, (hetero)aryl, or NH2, etc.; R2 is H, alkyl, (hetero)aryl, alkenyl, or perfluoroalkyl, etc.; R4 is naphthyl derivative], useful as inhibitors of plasminogen activator inhibitor-1 (PAI-1). For instance, naphthylbenzothiophene derivative II (59% inhibition at 25 μM) was prepared via heterocyclization of III with sodium azide with a yield of 49.8%.

L27 ANSWER 6 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:284147 HCAPLUS
DOCUMENT NUMBER: 142:355039
TITLE: Preparation of substituted aryloximes as inhibitors of PAI-1
INVENTOR(S): Havran, Lisa Marie; Butera, John Anthony; **Elokdah, Hassan Mahmoud**; Jenkins, Douglas John; Gundersen, Eric Gould
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 32 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005070584	A1	20050331	US 2004-948611	20040923
WO 2005030193	A1	20050407	WO 2004-US31460	20040924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-505801P P 20030925
US 2004-948611 A 20040923

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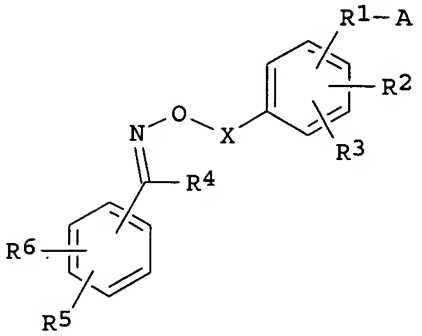


I

AB Title compds. I [R1 = bond, alkylene, etc.; R2-3 = H, halo, alkyl, etc.; R4 = H, (cyclo)alkyl; A = carboxy or acid mimic; X = (cyclo)alkylene, alkoxy; R5-6 = H, halo, alkyl, etc.] are prepared For instance, [4-[3-[[[1-(4-tert-butylphenyl)ethylidene]amino]oxy]propoxy]phenyl]acetic acid (II) is prepared from Me 4-hydroxyphenylacetic acid, 1,3-dibromopropane and 1-(4-tert-butylphenyl)ethanone oxime. At 25 μM, II exhibited 39% inhibition of PAI-1. I are useful for the treatment of, e.g., thrombosis.

L27 ANSWER 7 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:61463 HCAPLUS
DOCUMENT NUMBER: 142:309533
TITLE: Pharmacological Inhibition and Genetic Deficiency of Plasminogen Activator Inhibitor-1 Attenuates Angiotensin II/Salt-Induced Aortic Remodeling
AUTHOR(S): Weisberg, Alec D.; Albornoz, Francisco; Griffin, Jane P.; Crandall, David L.; **Elokdah, Hassan**; Fogo, Agnes B.; Vaughan, Douglas E.; Brown, Nancy J.
CORPORATE SOURCE: Department of Medicine, Divisions of Clinical Pharmacology, Vanderbilt University Medical Center, Nashville, TN, USA
SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology (2005), 25(2), 365-371
CODEN: ATVBFA; ISSN: 1079-5642
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective- To test the hypothesis that pharmacol. plasminogen activator inhibitor (PAI)-1 inhibition protects against renin-angiotensin-aldosterone system-induced cardiovascular injury, the effect of a novel

orally active small-mol. PAI-1 inhibitor, PAI-039, was examined in a mouse model of angiotensin (Ang) II-induced vascular remodeling and cardiac fibrosis. Methods and Results- Uninephrectomized male C57BL/6J mice were randomized to vehicle s.c., Ang II (1 μg/h) s.c., vehicle+PAI-039 (1 mg/g chow), or Ang II+PAI-039 during high-salt intake for 8 wk. Ang II caused significant medial, adventitial, and aortic wall thickening compared with vehicle. PAI-039 attenuated Ang II-induced aortic remodeling without altering the pressor response to Ang II. Ang II increased heart/body weight ratio and cardiac fibrosis. PAI-039 did not attenuate the effect of Ang II on cardiac hypertrophy and increased fibrosis. The effect of PAI-039 on Ang II/salt-induced aortic remodeling and cardiac fibrosis was comparable to the effect of genetic PAI-1 deficiency. Ang II increased aortic mRNA expression of PAI-1, collagen I, collagen III, fibronectin, osteopontin, monocyte chemoattractant protein-1, and F4/80. PAI-039 significantly decreased the Ang II-induced increase in aortic osteopontin expression at 8 wk. Conclusions- This study demonstrates that pharmacol. inhibition of PAI-1 protects against Ang II-induced aortic remodeling. Future studies are needed to determine whether the interactive effect of Ang II/salt and reduced PAI-1 activity on cardiac fibrosis is species-specific.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 8 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1025251 HCAPLUS
TITLE: Synthesis of a Biologically Active Naphthyl Benzofuran Derivative in Plasminogen Activator Inhibitor-1 (PAI-1) Program
AUTHOR(S): Wang, Zheng; **Elokdah, Hassan**; Antane, Madelene; McFarlane, Geraldine; Pan, Sherry
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Princeton, NJ, 08543, USA
SOURCE: Abstracts, 32nd Northeast Regional Meeting of the American Chemical Society, Rochester, NY, United States, October 31-November 3 (2004), GEN-095. American Chemical Society: Washington, D. C. CODEN: 69FWEU
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB A biol. active naphthyl benzofuran derivative 1 has been synthesized by two approaches: Approach I highlights Suzuki coupling of a benzofuran fragment and a naphthalene fragment followed by a regioselective acylation of the benzofuran derivative and a regioselective bromination of the biaryl analog. Approach II is more concise and it highlights a regioselective Suzuki coupling of a benzofuran and a dibromo substituted naphthalene, which shortened the synthesis. Approach II can be scaled up to 50.apprx.100 g (Hassan Elokdah, Geraldine McFarlane, Scott Mayer and David Crandall, US 6,599,925).

L27 ANSWER 9 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:762122 HCAPLUS
DOCUMENT NUMBER: 142:86256
TITLE: Characterization and comparative evaluation of a structurally unique PAI-1 inhibitor exhibiting oral in-vivo efficacy
AUTHOR(S): Crandall, D. L.; **Elokdah, H.**; Di, L.; Hennan, J. K.; Gorlatova, N. V.; Lawrence, D. A.
CORPORATE SOURCE: Cardiovascular and Metabolic Disease Research, Wyeth Research, Collegeville, PA, USA
SOURCE: Journal of Thrombosis and Haemostasis (2004), 2(8),

1422-1428
CODEN: JTHOA5; ISSN: 1538-7933
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Plasminogen activator inhibitor-1 (PAI-1) is the major physiol. inhibitor of both tissue-type plasminogen activator (tPA) and urokinase-type plasminogen activator (uPA). Elevated levels of PAI-1 are associated with thrombosis and vascular disease, suggesting that high plasma PAI-1 may promote a hypercoagulable state by disrupting the natural balance between fibrinolysis and coagulation. In this study, we identify WAY-140312 as a structurally novel small mol. inactivator of PAI-1, compare its inhibitory activity with other previously identified small mol. inhibitors, and investigate the mechanism of inactivation of PAI-1 in the presence of both tPA and uPA. In an immunofunctional assay, WAY-140312 inhibited PAI-1 with an estimated inhibitory concentration (IC50) of 11.7 μM, which was the lowest value obtained of the four different PAI-1 inactivators tested. Surface activity profiling indicated that the critical micelle concentration for WAY-140312 was 95.8 μM, and that each inhibitor exhibited unique phys. chemical properties. Using a sensitive direct activity assay, the IC50 for WAY-140312 was similar when either tPA or uPA was used as the target protease. Immunoblot anal. demonstrated that WAY-140312 near the IC50 inhibited the complex formation between either tPA or uPA and PAI-1. After oral administration, WAY-140312 exhibited 29% bioavailability with a plasma half-life of approx. 1 h. In an in-viva model of vascular injury, a 10 mg kg-1 oral dose of WAY-140312 was associated with improvement in arterial blood flow and reduction in venous thrombosis. Thus, WAY-140312 represents a structurally novel small mol. inhibitor of PAI-1, and is the first such mol. to exhibit efficacy in animal models of vascular disease following oral administration.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 10 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:658124 HCAPLUS
TITLE: Design, synthesis and SAR of substituted pyranoindoles as inhibitors of plasminogen activator inhibitor-1 (PAI-1) useful in the treatment of atherothrombosis and fibrinolytic disorders
AUTHOR(S): Li, David Z.; **Elokdah, Hassan**; McFarlane, Geraldine; Crandall, David L.
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Princeton, NJ, 08543, USA
SOURCE: Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), MEDI-260. American Chemical Society: Washington, D. C.
CODEN: 69FTZ8
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB High levels of plasminogen activator inhibitor-1 (PAI-1) have been associated with impaired fibrinolysis. PAI-1 has been implicated in a variety of chronic and acute diseases originating from fibrinolytic impairment such as deep vein thrombosis, coronary heart disease, pulmonary embolism, polycystic ovary syndrome, etc. Accordingly, agents that inhibit PAI-1 would be of utility in treating these disorders. We have developed a series of substituted indole carboxylic acid derivs. as PAI-1 inhibitors. The lead compound in the series, PAI-039 (1) is efficacious in the rat

thrombosis model when given orally at 1 mpk. Current work is focused on expanding the SAR of the indole series. Our goal is to discover potent and selective novel PAI-1 inhibitors. A series of pyranoindoles was explored. Compound (2) inhibited PAI-1 with an IC50 of 2.28 uM and was shown to have in vivo efficacy in the thrombosis model. Design, synthesis and SAR of this class of compds. as well as in vivo efficacy of the lead compound (2) will be presented.

L27 ANSWER 11 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:657007 HCAPLUS
TITLE: QSAR and molecular modeling studies of small molecule inhibitors of Plasminogen Activator Inhibitor-1
AUTHOR(S): Fan, Kristi Yi; **Elokdah, Hassan**; Crandall, David L.; Aulabaugh, Ann; Katz, Alan H.
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Princeton, NJ, 08543, USA
SOURCE: Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), COMP-169. American Chemical Society: Washington, D. C.
CODEN: 69FTZ8
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Plasminogen activator inhibitor-1 (PAI-1) is the major physiol. inhibitor of the serine proteases, tPA and uPA, and it is a major regulatory component of the plasminogen-plasmin system. Elevated plasma PAI-1 level is associated with decreased fibronolysis and increased risk of thrombosis and hyper-coagulation in a number of acute and chronic disorders. PAI-1 knock out mice are viable and protected from the development of atherosclerosis. Humans lacking the PAI-1 gene lead normal lives. These data suggest that modulation of PAI-1 activity offers a beneficial therapeutic for intervention in these diseases originating from fibrinolytic disorders. We present a unique approach to QSAR studies based on a data set of 90 inhouse compds. The IC50s are obtained from a kinetic assay in which the concentration of free PAI-1 is determined by monitoring the activity of tPA. A number of mol. descriptors were found to correlate with activity, and a corresponding pharmacophore model was developed using CATALYST.

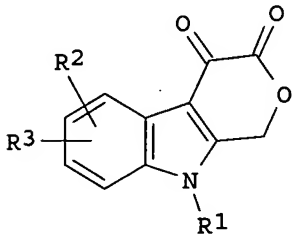
L27 ANSWER 12 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:515514 HCAPLUS
DOCUMENT NUMBER: 141:71529
TITLE: Preparation of substituted dihydropyranoindole-3,4-dione derivatives as inhibitors of plasminogen activator inhibitor-1 (PAI-1)
INVENTOR(S): **Elokdah, Hassan Mahmoud**; Li, David Zenan
PATENT ASSIGNEE(S): Wyeth, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052893	A2	20040624	WO 2003-US38932	20031209
WO 2004052893	A3	20040812		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-432327P P 20021210
OTHER SOURCE(S): MARPAT 141:71529
GI



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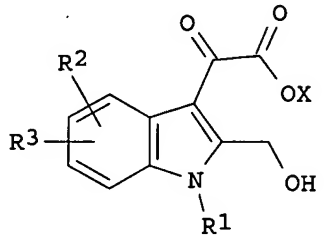

II

AB The title compds. [I and II; X = H, alkali metal or a basic amine moiety; R1 = alkyl, cycloalkyl, CH2(cycloalkyl), pyridinyl, CH2(pyridinyl), Ph, CH2Ph, the rings of these groups being optionally substituted; R2 = H, halo, alkyl, perfluoroalkyl, alkoxy, cycloalkyl, CH2(cycloalkyl), NH2, NO2; R3 = Ph, CH2Ph, OCH2Ph, pyridinyl, CH2(pyridinyl), etc., with the rings of these groups being optionally substituted] or a pharmaceutically acceptable salt or ester forms thereof, useful as inhibitors of plasminogen activator inhibitor-1 (PAI-1) for treating conditions resulting from fibrinolytic disorders such as deep vein thrombosis and coronary heart disease, and pulmonary fibrosis, were prepared E.g., a 7-step synthesis of 9-(4-methylbenzyl)-6-[4-(trifluoromethoxy)phenyl]-1,9-dihydropyrano[3,4-b]indole-3,4-dione II, starting from Et 5-bromo-1H-indole-2-carboxylate and 4-methylbenzyl bromide, was given. The compound II showed IC50 of 2.3 μM against human PAI-1. The pharmaceutical composition comprising the compound I is claimed.

L27 ANSWER 13 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:515481 HCAPLUS
DOCUMENT NUMBER: 141:71442
TITLE: Preparation of aryl, aryloxy, and alkyloxy substituted 1H-indol-3-yl glyoxylic acid derivatives as inhibitors of plasminogen activator inhibitor-1 (PAI-1)
INVENTOR(S): Jennings, Lee Dalton; **Elokdah, Hassan Mahmoud**; McFarlane, Geraldine Ruth
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004052854 A2 20040624 WO 2003-US38934 20031209
WO 2004052854 A3 20040805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004138283 A1 20040715 US 2003-731308 20031209
PRIORITY APPLN. INFO.: US 2002-432329P P 20021210
OTHER SOURCE(S): MARPAT 141:71442
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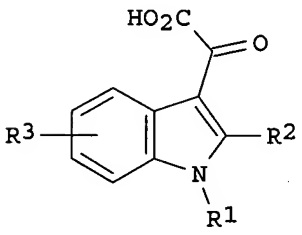

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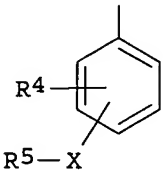

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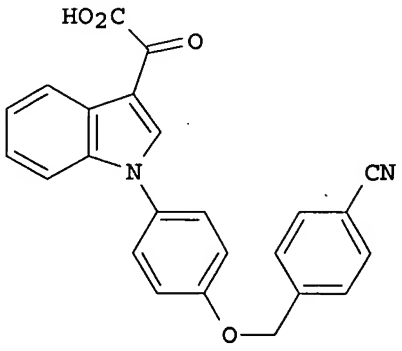


III

AB The title compds. [I; R1 = II (wherein R4 = H, halo, alkyl, etc.; X = O, S, NH; R5 = alkyl, perfluoroalkyl, cycloalkyl, etc.), alkyl, benzo[1,3]dioxol-5-ylmethyl, cycloalkylalkyl, etc.; R2 = H, alkyl, cycloalkyl, etc.; R3 = H, halo, alkyl, etc.], useful as inhibitors of plasminogen activator inhibitor (PAI-1) for treating conditions resulting from fibrinolytic disorders, such as deep vein thrombosis, coronary heart disease and pulmonary fibrosis, were prepared E.g., a 4-step synthesis of III, starting from indole and 4-iodoanisole, which showed 23% PAI-1 inhibition at 25 μM, was given. The pharmaceutical composition comprising the compound I is claimed.

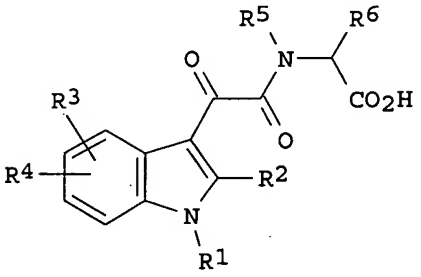
L27 ANSWER 14 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:493571 HCAPLUS
DOCUMENT NUMBER: 141:54194
TITLE: Preparation of substituted indolyloxoacetylaminoacetic acid derivatives as inhibitors of plasminogen

activator inhibitor-1 (PAI-1)
INVENTOR(S): **Elokdah, Hassan Mahmoud**; McFarlane, Geraldine Ruth; Li, David Zenan
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 13 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004116504	A1	20040617	US 2003-731074	20031209
WO 2004052856	A1	20040624	WO 2003-US38933	20031209

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-432331P P 20021210
OTHER SOURCE(S): MARPAT 141:54194
GI



I

AB The title compds. [I; R1 = alkyl, cycloalkyl, CH2(cycloalkyl), pyridinyl, CH2(pyridinyl), Ph, CH2Ph; R2 = H, alkyl, cycloalkyl, CH2(cycloalkyl), perfluoroalkyl; R3 = H, halo, alkyl, perfluoroalkyl, alkoxy, cycloalkyl, CH2(cycloalkyl), NH2 , NO2; R4 = Ph, CH2Ph, OCH2Ph, pyridinyl, CH2(pyridinyl); R5 = H, alkyl, cycloalkyl, CH2(cycloalkyl), perfluoroalkyl, aryl, alkylaryl; R6 = H, alkyl, hydroxyalkyl, 4-hydroxybenzyl, 3-indolylymethylene, 4-imidazolylmethylene, etc.; or R5 taken together with R6 = CH2CH2CH2] which are inhibitors of plasminogen activator inhibitor-1 (PAI-1) useful for treating fibrinolytic disorders, were prepared E.g., a multi-step synthesis of I [R1 = 4-tert-BuC6H4CH2; R2, R3 = H; R4 = 5-(3-MeC6H4); R5, R6 = H], starting from 5-bromoindole and 4-tert-butylbenzyl bromide, was given. The latter showed IC50 of 29 μM against PAI-1. The pharmaceutical composition comprising the compound I is claimed.

L27 ANSWER 15 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:459218 HCAPLUS

DOCUMENT NUMBER: 141:174039
TITLE: Tiplaxtinin, a Novel, Orally Efficacious Inhibitor of Plasminogen Activator Inhibitor-1: Design, Synthesis, and Preclinical Characterization
AUTHOR(S): **Elokdah, Hassan**; Abou-Gharbia, Magid; Hennan, James K.; McFarlane, Geraldine; Mugford, Cheryl P.; Krishnamurthy, Girija; Crandall, David L.
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Princeton, NJ, 08543, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(14), 3491-3494
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:174039

AB Indole oxoacetic acid derivs. were prepared and evaluated for in vitro binding to and inactivation of human plasminogen activator inhibitor-1 (PAI-1). SAR based on biochem., physiol., and pharmacokinetic attributes led to identification of tiplaxtinin as the optimal selective PAI-1 inhibitor. Tiplaxtinin exhibited in vivo oral efficacy in two different models of acute arterial thrombosis. The remarkable preclin. safety and metabolic stability profiles of tiplaxtinin led to advancing the compound to clin. trials.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 16 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:226448 HCAPLUS
TITLE: Mechanistic characterization of the interactions of plasminogen activator inhibitor-1 with a small molecule inhibitor using biophysical methods
AUTHOR(S): Krishnamurthy, Girija; Pitts, Keith; Smeltzer, Claudia; Ellestad, George; **Elokdah, Hassan**; Crandall, Dave
CORPORATE SOURCE: Screening Sciences, Wyeth Research, Pearl River, NY, 10965, USA
SOURCE: Abstracts of Papers, 227th ACS National Meeting, Anaheim, CA, United States, March 28-April 1, 2004 (2004), MEDI-090. American Chemical Society: Washington, D. C.
CODEN: 69FGKM
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB Plasminogen activator inhibitor (PAI-1) is the most important inhibitor of tissue-type plasminogen activator (tPA) and urokinase-type plasminogen activator (uPA). PAI-1, a 50- kDa glycoprotein is a member of the serpin family of inhibitors. It plays a major role in regulating fibrinolysis by inactivating tPA and uPA. PAI-1 is a metastable protein that exists in several distinct conformational states including the loop inserted inactive latent form. We have characterized the interactions of the small mol. inhibitor, WAY-555, with PAI-1 using biophys. methods. Fluorescence binding expts., using NBD-labeled PAI-1 show that the inhibitor binds PAI-1 with an affinity of ca.3 uM. WAY-555 inhibits the interaction of active PAI-1 with tPA due to the formation of cleaved form of PAI-1, as evidenced by the changes in thermal unfolding transitions of PAI-1 isoforms and gel mobility assays. WAY-555 does not induce the inactive latent form of PAI-1 or other polymerized forms of PAI-1. The implications of these findings with respect to the novel mechanism of action of WAY-555 will be discussed.

L27 ANSWER 17 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:226447 HCAPLUS
TITLE: Design, synthesis and SAR of 2-naphthyl benzofurans as inhibitors of plasminogen activator inhibitor-1
AUTHOR(S): **Elokdah, Hassan**; McFarlane, Geraldine R.; Krishnamurthy, Girija; Crandall, David L.
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Princeton, NJ, 08543, USA
SOURCE: Abstracts of Papers, 227th ACS National Meeting, Anaheim, CA, United States, March 28-April 1, 2004 (2004), MEDI-089. American Chemical Society: Washington, D. C.
CODEN: 69FGKM
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Plasminogen activator inhibitor-1 (PAI-1) is a major regulatory component of the plasminogen-plasmin system. PAI-1 is the principal physiol. inhibitor of both tissue type plasminogen activator (tPA) and urokinase type plasminogen activator (uPA). Elevated plasma levels of PAI-1 have been associated with thrombotic diseases. Neutralization of PAI-1 resulted in promotion of endogenous thrombolysis. Accordingly, agents that inhibit PAI-1 would be of utility in treating conditions originating from fibrinolytic disorder. High-throughput screening identified a benzoyl benzofuran hit. Subsequent substructure search and testing identified a series of naphthoyl benzofurans as more robust inhibitors of PAI-1. Synthetic efforts around the naphthoyl benzofurans led to the discovery of 2-naphthyl benzofuran series, with more potent in vitro and in vivo profiles, leading to the identifcation of WAY-164084 as a potent and selective PAI-1 inhibitor. This compound was subsequently advanced to pre-development status. The syntheses and SAR of these compds. as well as the binding properties and the in vivo activity of WAY-164084 in animal models of thrombosis will be presented.

L27 ANSWER 18 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:226446 HCAPLUS
TITLE: Design, synthesis and biological activity of a series of arylamide-naphthalen-2-yloxy-acidic derivatives as inhibitors of plasminogen activator inhibitor-1 (PAI-1), the major physiological inhibitor of tissue plasminogen activator (tPA)
AUTHOR(S): Commons, Thomas J.; Croce, Susan; Woodworth, Richard P.; Trybulski, Eugene J.; **Elokdah, Hassan**; Crandall, David L.; Hennan, James; Krishnamurthy, Girija; Mugford, Cheryl
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Collegeville, PA, 19426, USA
SOURCE: Abstracts of Papers, 227th ACS National Meeting, Anaheim, CA, United States, March 28-April 1, 2004 (2004), MEDI-088. American Chemical Society: Washington, D. C.
CODEN: 69FGKM
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Plasminogen activator inhibitor-1 (PAI-1) is the major physiol. inhibitor of tissue plasminogen activator (tPA), a serine proteinase involved in fibrinolysis. Epidemiol. studies have shown that elevated circulating levels of PAI-1 are associated with coronary heart disease and possibly atherosclerosis. These findings have generated an interest in developing a drug that specifically inhibits PAI-1. Consequently, high throughput

screening (HTS) of our compound bank led to a number of leads that were grouped into eight distinct series. One such series ultimately led to the benzofuran amide A, one of five compds. selected as a Late Stage Discovery compound The SAR leading to A, synthetic routes to various targets and the biol. activity of selected compds. will be discussed.

L27 ANSWER 19 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:226445 HCAPLUS
TITLE: Design and synthesis of novel oxime-based PAI-1 inhibitors
AUTHOR(S): Havran, Lisa M.; Butera, John A.; Jenkins, Douglas; **Elokdah, Hassan**; Krishnamurthy, Girija; Crandall, David L.
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Princeton, NJ, 08543, USA
SOURCE: Abstracts of Papers, 227th ACS National Meeting, Anaheim, CA, United States, March 28-April 1, 2004 (2004), MEDI-087. American Chemical Society: Washington, D. C.
CODEN: 69FGKM
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Plasminogen Activator Inhibitor-1 (PAI-1), a member of the Serine Protease Inhibitor (SERPIN) family, is the most important physiol. inhibitor of tissue-type plasminogen activator (tPA) and urokinase-type plasminogen activator (uPA). Elevated PAI-1 activity is associated with decreased fibrinolysis and increased risk of thrombosis in many chronic and acute disease states. As part of a program to find an orally active small mol. that would normalize plasma PAI-1 activity and reduce thrombotic risk, high throughput screening was completed on the Wyeth chemical library. Several chemical leads were found including a bisphenoxy series exemplified by 1. Patent and stability issues were addressed by the development of a series of oxime based analogs. Benzofuran 2 improves the in vitro potency of previous leads and shows in vivo efficacy at 5 mpk in a clot lysis model. Recent results from this work will be presented.

L27 ANSWER 20 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:226372 HCAPLUS
TITLE: Tiplaxtinin: A novel orally efficacious inhibitor of PAI-1 for use in treatment of diseases of fibrinolytic dysfunction
AUTHOR(S): **Elokdah, Hassan**; McFarlane, Geraldine R.; Li, David Z.; Butera, John A.; Abou-Gharbia, Magid; Krishnamurthy, Girija; Hennan, James; Friedrichs, Gregory; Crandall, David L.
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Princeton, NJ, 08543, USA
SOURCE: Abstracts of Papers, 227th ACS National Meeting, Anaheim, CA, United States, March 28-April 1, 2004 (2004), MEDI-014. American Chemical Society: Washington, D. C.
CODEN: 69FGKM
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB The serine protease inhibitor plasminogen activator inhibitor-1 (PAI-1) regulates fibrinolysis through its modulation of plasmin, and increased plasma PAI-1 is associated with diseases of fibrinolytic impairment. PAI-1 is the physiol. inhibitor of both urokinase plasminogen activator (uPA) and tissue plasminogen activator (tPA), and its elevation is associated with clot stabilization in acute thrombosis as well as tissue remodeling

occurring during atherosclerosis and cancer. The central role of plasmin in these diverse diseases suggests that inhibition of PAI-1 has potential therapeutic benefit, yet an orally active PAI-1 inhibitor has not yet been described. We present the discovery of Tiplaxtinin, a novel indole-oxoacetic acid derivative that both binds PAI-1 with high affinity (Kd=480 nM) and exhibits oral efficacy in preclin. models of arterial and venous thrombosis. We also describe the synthesis and structure-activity relationship studies leading to the discovery of Tiplaxtinin, the biol. data predictive of its utility, and the preclin. safety assessment leading to its selection as a clin. candidate.

L27 ANSWER 21 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:1011633 HCAPLUS
DOCUMENT NUMBER: 140:181384
TITLE: Design, Synthesis, and Biological Evaluation of Thio-Containing Compounds with Serum HDL-Cholesterol-Elevating Properties
AUTHOR(S): **Elokdah, Hassan**; Sulkowski, Theodore S.; Abou-Gharbia, Magid; Butera, John A.; Chai, Sie-Yearl; McFarlane, Geraldine R.; McKean, Mar-Lee; Babiak, John L.; Adelman, Steven J.; Quinet, Elaine M.
CORPORATE SOURCE: Medicinal Chemistry, Wyeth Research, Princeton, NJ, 08543, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(3), 681-695
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel series of substituted sulfanyldihydroimidazolones that modulates high-d. lipoprotein cholesterol (HDL-C) has been reported to have HDL-elevating properties in several animal models. Concerns about the chemical and metabolic stability of these compds. directed us to explore the structure-activity relationship (SAR) of a related series of substituted thiohydantoins. Expansion of the scope of the thiohydantoin series led to exploration of compds. in related thio-containing ring systems and the N-cyanoguanidine derivative Compds. were tested sequentially in three animal models to assess their HDL-C elevating efficacy and safety profiles. Further evaluation of selected compds. in a dose-response paradigm culminated in the identification of one of the major products as a candidate compound for advanced preclin. studies.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 22 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:883121 HCAPLUS
DOCUMENT NUMBER: 140:139089
TITLE: WAY-140312 reduces plasma PAI-1 while maintaining normal platelet aggregation
AUTHOR(S): Crandall, David L.; Hennan, James K.; **Elokdah, Hassan**; Krishnamurthy, Girija; Antrilli, Thomas M.; Bauer, Jean S.; Morgan, Gwen A.; Swillo, Robert E.
CORPORATE SOURCE: Cardiovascular and Metabolic Diseases Research, Wyeth Research, Collegeville, PA, 19426, USA
SOURCE: Biochemical and Biophysical Research Communications (2003), 311(4), 904-908
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Plasminogen activator inhibitor-1 (PAI-1) is the major physiol. inhibitor

of tissue plasminogen activator (tPA) and is elevated in diseases of vascular remodeling. In this study, we describe an inhibitor of active PAI-1, WAY-140312. Using fluorescence spectroscopy, it was determined that WAY-140312 bound PAI-1 at a single binding site with a dissociation constant of 5 μM. In a biochem. assay determining direct tPA activity, human recombinant PAI-1 completely inhibited tPA, but this inhibition was blocked by WAY-140312 at an IC50 of 15.6 μM. In vivo, a 10 mg/kg oral dose of WAY-140312 to rats produced a significant plasma reduction of active PAI-1. Bleeding time, thrombin clotting time, and ex vivo platelet aggregation induced by ADP (20 μM) or collagen (2.5 μg/mL) were not affected by administration of WAY-140312. These results are the first to demonstrate that an orally active PAI-1 inhibitor can reduce plasma PAI-1 activity while maintaining normal platelet aggregation and coagulation.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 23 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:492714 HCAPLUS
DOCUMENT NUMBER: 139:69265
TITLE: Preparation of 1,3-disubstituted-2-thioxoimidazolidine-4,5-diones as potassium channel openers
INVENTOR(S): Butera, John A.; **Elokdah, Hassan M.**; Sulkowski, Theodore S.; Primeau, John L.; Lennox, Joseph R.
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003119890	A1	20030626	US 2002-282540		20021029
PRIORITY APPLN. INFO.:			US 2001-340921P	P	20011030

OTHER SOURCE(S): MARPAT 139:69265
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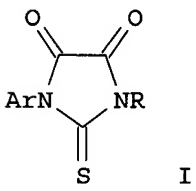


I

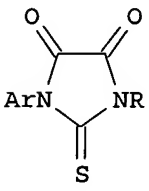
AB Title compds. (I; R = (branched) alkyl; Ar = Ph, Ph substituted with ≥1 halo, alkyl, alkoxy, alkylthio, alkylamino, cyano, perfluoroalkoxy, heteroaryl), were prepared Thus, 4-cyanophenyl isothiocyanate in THF at room temperature was treated with a solution of 3,3-dimethyl-2-aminobutane in THF and the reaction was stirred overnight at room temperature to afford 96% 1-(4-cyanophenyl)-3-(1,2,2-trimethylpropyl)thiourea. Et chlorooxoacetate was added to a stirring solution of the above thiourea in CH2Cl2 and the resulting mixture was stirred

overnight at room temperature to give 73% 4-[4,5-dioxo-2-thioxo-3-(1,2,2-trimethylpropyl)imidazolidin-1-yl]benzonitrile. The latter inhibited contractions in rat bladder strips with IC50 = 3.3 μM.

L27 ANSWER 24 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:492713 HCAPLUS
DOCUMENT NUMBER: 139:69264
TITLE: Preparation of 1,3-disubstituted-2-thioxoimidazolidine-4,5-diones for the treatment of atherosclerosis
INVENTOR(S): **Elokdah, Hassan M.**; Sulkowski, Theodore S.
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003119889	A1	20030626	US 2002-282511		20021029
PRIORITY APPLN. INFO.:			US 2001-341046P	P	20011030

OTHER SOURCE(S): MARPAT 139:69264
GI



I

AB Antiatherosclerotic title compds. (I; R = alkyl, alkenyl, alkynyl, O(CH2)nCO2R'; R' = alkyl; n = 1-3; Ar = Ph, Ph substituted with ≥1 halo, alkyl, alkenyl, alkynyl, alkoxy, perfluoroalkyl, perfluoroalkoxy, alkylthio), were prepared Thus, Et chlorooxoacetate was added dropwise to Et 2-[[[(5-chloro-2-methylanilino)carbothioyl]amino]oxy]acetate (preparation given) in methylene chloride the mixture was refluxed 1 h to give Et 2-[[3-(5-chloro-2-methylphenyl)-4,5-dioxo-2-thioxo-1-imidazolidinyl]oxy]acetate. The latter at 100 mg/kg orally in rats increased HDL cholesterol by 242%.

L27 ANSWER 25 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:323274 HCAPLUS
DOCUMENT NUMBER: 139:145710
TITLE: Mapping of a Conformational Epitope on Plasminogen Activator Inhibitor-1 by Random Mutagenesis
AUTHOR(S): Gorlatova, Natalia V.; **Elokdah, Hassan**; Fan, Kristi; Crandall, David L.; Lawrence, Daniel A.
CORPORATE SOURCE: The Holland Laboratory, Department of Vascular Biology, American Red Cross, Rockville, MD, 20855, USA
SOURCE: Journal of Biological Chemistry (2003), 278(18), 16329-16335
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology

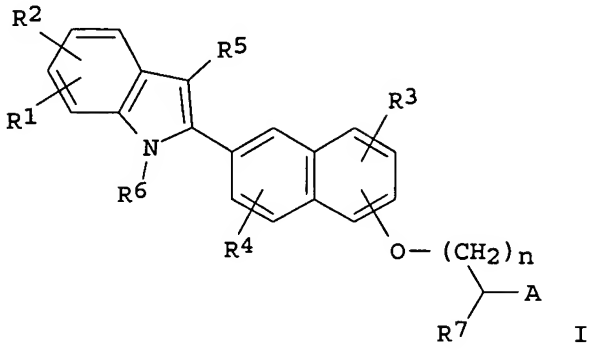
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mechanism for the conversion of plasminogen activator inhibitor-1 (PAI-1) from the active to the latent conformation is not well understood. Recently, a monoclonal antibody, 33B8, was described that rapidly converts PAI-1 to the latent conformation (Verhamme, I., Kvassman, J. O., Day, D., Debrock, S., Vleugels, N., Declerck, P. J., and Shore, J. D. (1999) J. Biol. Chemical 274, 17511-17517). In an attempt to understand this interaction, and more broadly to understand the mechanism of the natural transition of PAI-1 to the latent conformation, we have used random mutagenesis to identify the 33B8 epitope in PAI-1. This site involves at least 8 amino acids scattered over more than two-thirds of the linear sequence that form a compact epitope on the PAI-1 three-dimensional structure. Surface plasmon resonance studies indicate a high affinity interaction between latent PAI-1 and 33B8 that is .apprx.100-fold higher than comparable binding to active PAI-1. Structural modeling results together with surface plasmon resonance anal. of parental and site-directed PAI-1 mutants with disrupted 33B8 binding suggest the existence of a specific PAI-1 intermediate structure that is stabilized by 33B8 binding. These analyses strongly suggest that this intermediate form of PAI-1 has a partial insertion of the reactive center loop into β-sheet A, and together, these data have significant implications for the general serpin mechanism of proteinase inhibition.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 26 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:5953 HCAPLUS
DOCUMENT NUMBER: 138:73173
TITLE: Preparation of substituted 2-(2-naphthyl)indoles as inhibitors of plasminogen activator inhibitor type-1 (PAI-1)
INVENTOR(S): Mayer, Scott Christian; Gundersen, Eric Gould; **Elokdah, Hassan Mahmoud**; Crandall, David Leroy
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000684	A1	20030103	WO 2002-US21113	20020618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003032626	A1	20030213	US 2002-171041	20020613
US 6800654	B2	20041005		
CA 2448798	AA	20030103	CA 2002-2448798	20020618
EP 1397356	A1	20040317	EP 2002-746846	20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

BR 2002010504	A	20040518	BR 2002-10504		20020618
JP 2004534825	T2	20041118	JP 2003-507087		20020618
US 2004266733	A1	20041230	US 2004-894618		20040720
PRIORITY APPLN. INFO.:			US 2001-299651P	P	20010620
			US 2002-171041	A1	20020613
			WO 2002-US21113	W	20020618

OTHER SOURCE(S): MARPAT 138:73173
GI



I

AB The title compds. [I; R1-R4 = H, alkyl, alkanoyl, etc.; R5 = H, alkyl, perfluoroalkyl, etc.; R6 = H, alkyl, alkylaryl, etc.; R7 = H, alkyl, alkylaryl, (un)substituted aryl; n = 0-6; A = CO2H, or an acid mimic such as tetrazole, SO3H, PO3H2, tetronic acid, etc.], useful for the treatment of thrombosis or fibrinolytic impairment in a mammal, were prepared E.g., a 7-step synthesis of 1-benzyl-3-pentyl-2-[6-(1H-tetrazol-5-ylmethoxy)-2-naphthyl]-1H-indole, starting from 6-methoxy-2-naphthaldehyde and hexylmagnesium bromide, which showed IC50 of 9.85 μM against PAI-1 in the antibody assay, was given.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 27 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:5942 HCAPLUS
DOCUMENT NUMBER: 138:73168
TITLE: Preparation of naphthylbenzofurans as inhibitors of plasminogen activator inhibitor-1 (PAI-1).
INVENTOR(S): **Elokdah, Hassan Mahmoud**; Mcfarlane, Geraldine Ruth; Mayer, Scott Christian; Crandall, David Leroy
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

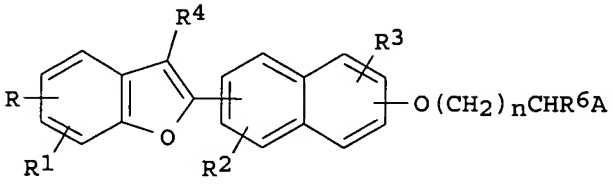
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000671	A1	20030103	WO 2002-US19231	20020618

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2449844	AA	20030103	CA 2002-2449844		20020618
US 2003018067	A1	20030123	US 2002-174166		20020618
US 6599925	B2	20030729			
EP 1401822	A1	20040331	EP 2002-747904		20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2002010532	A	20040622	BR 2002-10532		20020618
JP 2004534824	T2	20041118	JP 2003-507076		20020618
PRIORITY APPLN. INFO.:			US 2001-299702P	P	20010620
			WO 2002-US19231	W	20020618

OTHER SOURCE(S): MARPAT 138:73168
GI



I

AB Title compds. [I; R-R3 = H, alkyl, cycloalkyl, cycloalkylmethyl, alkanoyl, halo, OH, (substituted) aryl, heteroaryl, perfluoroalkyl, alkoxy, amino, perfluoroalkoxy; R4 = H, alkyl, perfluoroalkyl, (substituted) aryl, heteroaryl, alkenyl, alkenylaryl, aryl, CH2R5, CH(OH)R5, COR5, CH(SH)R5, G(S)R5; R5 = H, alkyl, perflouroalkyl, (substituted) aryl, heteroaryl, alkenyl, alkenylaryl; R6 = H, alkyl, cycloalkyl, -CH2-cycloalkyl, alkylaryl, aryl, substituted aryl, heteroaryl, or substituted heteroaryl; n = 0-6; A = CO2H, acid mimic], were prepared Thus, 2-[[1-bromo-6-(3-pentanoyl-1-benzofuran-2-yl)-2-naphthyl]oxy]acetonitrile (preparation given), NaN3, and NH4Cl in DMF were heated at 80° for 2 h to give 1-[2-[5-Bromo-6-(1H-1,2,3,4-tetrazol-5-ylmethoxy)-2-naphthyl]-1-benzofuran-3-yl]-1-pentanone. The latter inhibited PAI-1 with IC50 = 7.7 μM. I are useful in treating fibrinolytic disorders such as deep vein thrombosis, coronary heart disease, and pulmonary fibrosis.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

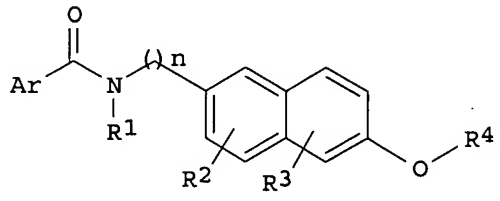
L27 ANSWER 28 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2003:5921 HCAPLUS
DOCUMENT NUMBER:	138:55749
TITLE:	Preparation of 6-arylamido(methyl)-naphthalen-2-yloxy-acetic acid derivatives as inhibitors of plasminogen activator inhibitor type-1 (PAI-1)
INVENTOR(S):	Commons, Thomas Joseph; Croce, Susan Christman; Woodworth, Richard Page; Trybulski, Eugene John; **Elokdah, Hassan Mahmoud**; Crandall, David Leroy
PATENT ASSIGNEE(S):	Wyeth, John, and Brother Ltd., USA
SOURCE:	PCT Int. Appl., 146 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003000649	A1	20030103	WO 2002-US19193		20020618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
TW 591020	B	20040611	TW 2002-91112528		20020610
US 2003045560	A1	20030306	US 2002-170558		20020613
US 6589970	B2	20030708			
CA 2450174	AA	20030103	CA 2002-2450174		20020618
EP 1397341	A1	20040317	EP 2002-746561		20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2002010468	A	20040810	BR 2002-10468		20020618
JP 2004536091	T2	20041202	JP 2003-506853		20020618
PRIORITY APPLN. INFO.:			US 2001-299652P	P	20010620
			US 2001-308656P	P	20010730
			WO 2002-US19193	W	20020618

OTHER SOURCE(S): MARPAT 138:55749
GI



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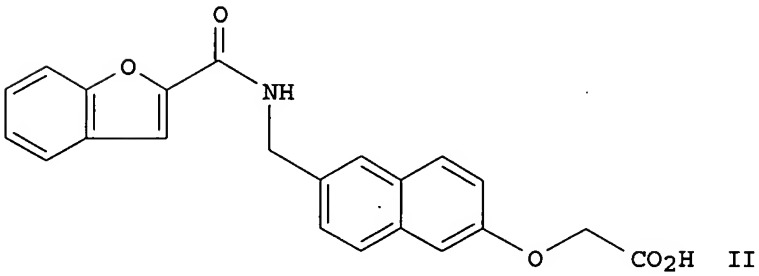


II

AB Title compds. I [Ar = Ph, naphthyl, furanyl, etc.; R1 = H, alkyl, Ph, etc.; R2-3 = H, alkyl, Ph, halo, etc.; R4 = CHR5CO2H, CH2tetrazole, etc.; n = 0-1; R5 = H, benzyl] are prepared For instance, ((6-hydroxynaphthalen-2-yl)methyl)ammonium bromide (preparation given) and benzofuran-2-carbonyl chloride were coupled to form the corresponding amide. The intermediate

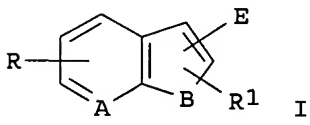
amide was alkylated with Me bromoacetate (DMF, K2CO3) and the resulting alkylation produce saponified to give II. II at 100 μM exhibited 25% inhibition of PAI-1. I are useful for the treatment of non-insulin dependent diabetes.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 29 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:5777 HCAPLUS
DOCUMENT NUMBER: 138:78453
TITLE: Aryloxy-acetic acid compounds useful as inhibitors of plasminogen activator inhibitor-1 (PAI-1)
INVENTOR(S): **Elokdah, Hassan Mahmoud**
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000258	A1	20030103	WO 2002-US19240	20020618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003013732	A1	20030116	US 2002-171056	20020613
PRIORITY APPLN. INFO.:			US 2001-299659P P	20010620

OTHER SOURCE(S): MARPAT 138:78453
GI



I

AB This invention provides methods of inhibiting plasminogen activator inhibitory (PAI-1) in a mammal, utilizing compds. of the formula (I) wherein: A is C or N; B is O, S, N, or CH=CH; and E is aryl or heterocycle.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 30 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:5772 HCAPLUS
DOCUMENT NUMBER: 138:73172
TITLE: Preparation of substituted indole-3-acetic acids as inhibitors of plasminogen activator inhibitor-1 (PAI-1)
INVENTOR(S): **Elokdah, Hassan Mahmoud**; Mcfarlane,

Geraldine Ruth; Li, David Zenan; Jennings, Lee Dalton; Crandall, David Leroy

PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000253	A1	20030103	WO 2002-US19344	20020618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003125371	A1	20030703	US 2002-174159	20020618
EP 1397130	A1	20040317	EP 2002-744425	20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004534817	T2	20041118	JP 2003-506899	20020618
PRIORITY APPLN. INFO.:			US 2001-299657P P	20010620
			WO 2002-US19344 W	20020618

OTHER SOURCE(S): MARPAT 138:73172
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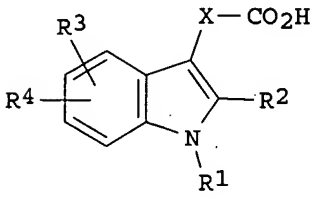

I

AB The title compds. [I; X = a bond, CH2, CO; R1 = alkyl, cycloalkyl, CH2(cycloalkyl), pyridinyl, CH2(pyridinyl), Ph, CH2Ph; R2 = H, alkyl, cycloalkyl, CH2(cycloalkyl), perfluoroalkyl; R3 = H, halo, alkyl, perfluoroalkyl, alkoxy, cycloalkyl, CH2(cycloalkyl), NH2, NO2; R4 = (un)substituted Ph, CH2Ph, OCH2PH, pyridinyl, CH2(pyridinyl)] or their salts or ester forms, useful as inhibitors of plasminogen activator inhibitor-1 (PAI-1) for treating conditions resulting from fibrinolytic disorders such as deep vein thrombosis and coronary heart disease, and pulmonary fibrosis, were prepared E.g., a 4-step synthesis of I [X = CO; R1 = Me; R2-R3 = H; R4 = 6-[4-(trifluoromethoxy)phenyl]], starting from 6-bromo-1H-indole and 4-trifluoromethoxyphenylboronic acid, which showed 15% inhibition of PAI-1 at 25 μM, was given.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 31 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:510506 HCAPLUS
DOCUMENT NUMBER: 138:180405
TITLE: Novel human metabolites of the angiotensin-II antagonist tasosartan and their pharmacological effects
AUTHOR(S): **Elokdah, Hassan M.**; Friedrichs, Gregory S.; Chai, Sie-Yearl; Harrison, Boyd L.; Primeau, John; Chlenov, Michael; Crandall, David L.
CORPORATE SOURCE: Chemical Sciences, Medicinal Chemistry, Wyeth Research, Princeton, NJ, 08543, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(15), 1967-1971
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three novel metabolites of the angiotensin-II (A-II) receptor antagonist tasosartan have been identified in humans, and the syntheses and pharmacol. profiling of these metabolites are reported. Each metabolite bound the human A-II receptor with IC50s between 20 and 45 nM. The in vivo effects of these compds. in attenuating the pressor response to angiotensin-II challenge in anesthetized rats were also investigated. An unsatd. diol metabolite exhibited in vivo efficacy at i.v. doses of 1 and 3 mg/kg, while the other metabolites, both carboxylic acids, had no significant effect at the same doses.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 32 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:392236 HCAPLUS
DOCUMENT NUMBER: 136:386134
TITLE: Preparation of imidazo-isoquinolin-5-ones, pyrimido-isoquinolin-6-ones and imidazo-naphthyridin-5-ones as antiatherosclerotics
INVENTOR(S): **Elokdah, Hassan M.**; Sulkowski, Theodore S.; Chai, Sie-Yearl; Babiak, John
PATENT ASSIGNEE(S): American Home Products Corporation, USA; Wyeth
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002061900	A1	20020523	US 2001-965957	20010928
US 6448255	B2	20020910		
PRIORITY APPLN. INFO.:			US 2000-237304P P	20001002
OTHER SOURCE(S):	MARPAT 136:386134			

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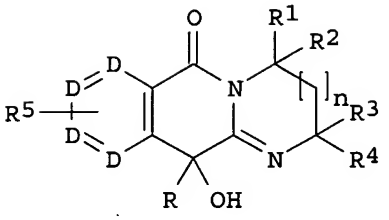

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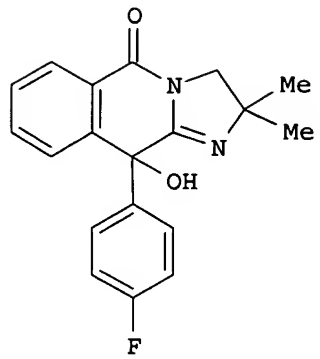


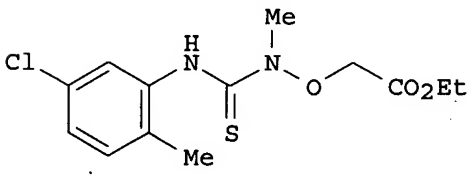
II

AB The title compds. [I; R = H, alkyl, alkenyl, alkynyl, (un)substituted (hetero)aryl; D = CH, carbon bound to R5, N; R1-R4 = H, alkyl, or taken together form a ring; R5 = H, alkyl, alkenyl, alkynyl, aryl, hydroxy, alkoxy, perfluoroalkyl, perfluoroalkoxy, alkylthio, NO2, NH2, mono or di-alkylamino, halo; n = 0-3] which increase HDL cholesterol concns., were prepared Thus, reacting 1-(4-fluorophenyl)-3-oxo-1,3-dihydro-isobenzofuran-1-carboxamide (preparation given) with 2-methyl-1,2-diaminopropane in PhMe afforded II which showed 90% HDL cholesterol level increase in blood serum at 100 mg/kg/day.

L27 ANSWER 33 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:294263 HCAPLUS
DOCUMENT NUMBER: 136:309767
TITLE: Preparation of amino thioxomethyl amino oxyacetic acid derivatives as antiatherosclerotics
INVENTOR(S): **Elokdah, Hassan M.**; Sulkowski, Theodore S.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002045776	A1	20020418	US 2001-965898		20010928
US 6472430	B2	20021029			
PRIORITY APPLN. INFO.:			US 2000-237466P	P	20001002

OTHER SOURCE(S): MARPAT 136:309767
GI



I

AB The title compds. ArNHC(:S)NROCR2R3COR1 [R = alkyl; R1 = OH, NH2, alkoxy;

R2, R3 = H, alkyl, aryl; Ar = (un)substituted Ph, indanyl, benzhydryl], useful as antiatherosclerotics, were prepared Thus, reacting 5-chloro-2-methylphenyl isothiocyanate with Et N-methylaminooxyacetate (preparation given) in ether afforded I which showed 118% HDL cholesterol increase at 100 mg/kg in rats.

L27 ANSWER 34 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:275976 HCAPLUS
DOCUMENT NUMBER: 136:309940
TITLE: Preparation of 3-thioxo[1,2,4]oxadiazinan-5-ones as antiatherosclerotic agents
INVENTOR(S): **Elokdah, Hassan Mahmoud**; Sulkowski, Theodore Sylvester
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028845	A1	20020411	WO 2001-US30588	20010928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001094910	A5	20020415	AU 2001-94910	20010928
US 2002061883	A1	20020523	US 2001-965874	20010928
US 6562814	B2	20030513		

PRIORITY APPLN. INFO.: US 2000-237468P P 20001002
WO 2001-US30588 W 20010928
OTHER SOURCE(S): MARPAT 136:309940
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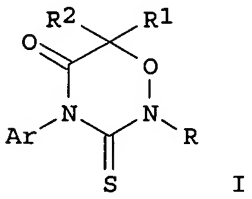


I

AB The title compds. [I; R = alkyl, alkenyl, alkynyl; R1, R2 = H, alkyl, aryl; Ar = (un)substituted Ph, indanyl, benzhydryl] that elevate HDL cholesterol concentration, and which may be useful for the treatment of atherosclerotic conditions such as coronary heart disease, were prepared Thus, reacting 4-chloro-2-methylphenyl isothiocyanate with N-methylaminoxyacetic acid hydrochloride (preparation given) in the presence of Et3N in CHCl3 followed by cyclizing the resulting acid with PCl5 in C6H6 afforded I [R = Me; R1, R2 = H; Ar = 4-chloro-2-methylphenyl], which

produced a 221% HDL cholesterol increase at 100 mg/kg/day.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

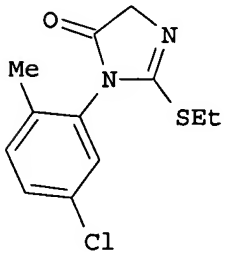
L27 ANSWER 35 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:640782 HCAPLUS
TITLE: Design and synthesis of thioxo-imidazolidinediones and derivatives as high density lipoprotein cholesterol (HDL-C) enhancers
AUTHOR(S): **Elokdah, Hassan**; Sulkowski, Theodore; Chai, Sie-Yearl; McFarlane, Geraldine R.; Butera, John A.; McKean, Mar-Lee; Quinet, Elaine
CORPORATE SOURCE: Chemical Sciences, Wyeth-Ayerst Research, Princeton, NJ, 08543, USA
SOURCE: Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), ORGN-419. American Chemical Society: Washington, D. C.
CODEN: 69BUZP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Epidemiol. studies have revealed trends correlating the elevation of high d. lipoprotein cholesterol (HDL-C), with decreased incidence of atherosclerosis and coronary heart disease (CHD). Functionally, HDL-C acts as a transporter of cholesterol from the peripheral tissues to the liver where it is catabolized and excreted. Thus, agents that increase HDL-C should be useful therapuetics for the treatment of atherosclerosis and CHD. A series of 2-substituted-sulfanyl-3,5-dihydro-imidazole-4-ones (1) and 2-substituted-sulfanyl-1H-imidazole-4,5-diones were prepared and were shown to increase high d. lipoprotein cholesterol over other lipid fractions. Compds. of this class were show to be extensively metabolized. Synthesis and structure assignment of a major metabolite of the ethyl-sulfanyl lead will be reported. Concerns about the chemical and metabolic stability of these classes of compds. directed our efforts to a related series of substituted thiohydantoin derivs. (2). These compds. were also effective in raising HDL-C over other lipid fractions and offered improved stability and metabolic profiles. However, the detection of a thiourea metabolite prompted us to investigate systems with potentially different metabolic fates such as substituted thiouracil, substituted thiopiperazinone, and substituted 3-thioxo-[1,2,4]-oxadiazinan-5-one (3). Synthesis and structure activity relationship (SAR) of these series derivs. will be discussed.

L27 ANSWER 36 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:118615 HCAPLUS
DOCUMENT NUMBER: 134:326486
TITLE: Design and synthesis of tricyclic derivatives as high density lipoprotein cholesterol enhancers
AUTHOR(S): **Elokdah, H.**; Chai, S.-Y.; Ho, D.; Sulkowski, T.
CORPORATE SOURCE: Chemical Sciences, Wyeth-Ayerst Research, Princeton, NJ, 08543, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(3), 339-342
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:326486
AB A pharmacophore for increasing HDLC was proposed based on common

structural features of non-thio-containing compds. with HDLC enhancing properties. A search of the compound database identified various series of these non-thio-containing compds., including a novel tricyclic imidazoisoquinolinone. Preparation of 1-aryl-3-oxo-1,3-dihydro-2-benzofuran-1-carboxamides using a novel and widely applicable one-step process from 2-acylbenzoic acids is reported. Reaction of diamines with 1-aryl-3-oxo-1,3-dihydro-2-benzofuran-1-carboxamides and related aza-analogs proceeded regioselectively to furnish imidazoisoquinolinones, pyrimidoisoiquinolinones and imidazonaphthyridines. Compds. of these series increased concns. of HDLC in test animals following oral administration.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 37 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:565879 HCAPLUS
DOCUMENT NUMBER: 133:329355
TITLE: Effects of 2-(substituted-sulfanyl)-3,5-dihydro-imidazole-4-one and 2-(substituted-sulfanyl)-1H-imidazole-4,5-dione derivatives on serum HDL-cholesterol
AUTHOR(S): **Elokdah, H.**; Sulkowski, T.; Cochran, D.; McKean, M.-L.; Quinet, E.
CORPORATE SOURCE: CN 8000, Chemical Sciences, Medicinal Chemistry, Wyeth-Ayerst Research, Princeton, NJ, 08543, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(16), 1791-1794
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A series of 2-substituted sulfanyl-3,5-dihydro-imidazole-4-ones and 2-substituted sulfanyl-1H-imidazole-4,5-diones was prepared and shown to increase high d. lipoprotein cholesterol over other lipid fractions. Compound (I) showed efficacy in addnl. animal models. The major metabolite of I was isolated and its synthesis is reported. The effects of the metabolite on the lipid profile in rats were investigated.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 38 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:617406 HCAPLUS
TITLE: Benzylamino analogs of 1,2-diaminocyclobutene-3,4-dione as novel KATP-channel openers targeted for treatment of urge urinary incontinence.

AUTHOR(S): McFarlane, Geraldine R.; Gundersen, Eric G.; **Elokdah, Hassan**; Herbst, David R.; Antane, Madelene M.; Hirth, Bradford H.; Butera, John A.; Graceffa, Russell F.; Quagliato, Dominick A.; Matelan, Edward; Gilbert, Adam M.; Francisco, Gerardo P.; Argentieri, Thomas; Norton, N. Wesley; Warga, Dawn M.; Sheldon, Jeffery; Wojdan, Alexandra; Freeden, Chris; Woods, Morgan

CORPORATE SOURCE: Chemical Sciences, Wyeth-Ayerst Research, Princeton, NJ, 08543-8000, USA

SOURCE: Book of Abstracts, 218th ACS National Meeting, New Orleans, Aug. 22-26 (1999), MEDI-035. American Chemical Society: Washington, D. C.
CODEN: 67ZJA5

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Diverse number of potassium channels have been described in the literature. Of these the ATP-sensitive potassium channel (K channel) has been targeted and modulated for the regulation of a wide range of physiol. processes, among which is the mediation of smooth muscle cell contractility. K channel activators (KCAs)/openers (KCOs) induce hyperpolarization of cell membranes leading to smooth muscle cell relaxation. A variety of structurally diverse KCOs have been reported. A bladder selective KCO can potentially alleviate bladder instability and may be useful for the treatment of urge urinary incontinence (UUI) without concomitant hemodynamic effects. Replacement of the N-cyanoguanidine moiety of Pinacidil (1) with a 1,2-diaminocyclobutenedione (squarate diamine) led us to the identification of a series of N-aryl-N"-alkyl diamino squarates (2) as bladder selective KCOs. To further improve the metabolic stability of this class of compds., a series of N-benzyl-N"-alkyl diamino squarates (3) were prepared and were found to be potent and bladder selective KCOs. The synthesis, SAR, and activity of selected agents will be presented.

L27 ANSWER 39 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:521438 HCAPLUS

DOCUMENT NUMBER: 131:144521

TITLE: Preparation of 2-substituted-1-acyl-1,2-dihydroquinolines with high-density lipoprotein cholesterol-elevating and antiatherosclerotic properties

INVENTOR(S): Babiak, John; **Elokdah, Hassan Mahmoud**; Miller, Christopher Paul; Sulkowski, Theodore Sylvester

PATENT ASSIGNEE(S): American Home Products Corporation, USA

SOURCE: U.S., 6 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

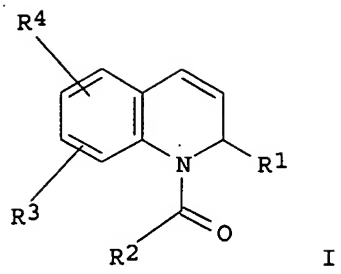
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 5939435	A	19990817	US 1998-15178		19980129
PRIORITY APPLN. INFO.:			US 1997-37409P	P	19970203

OTHER SOURCE(S): CASREACT 131:144521; MARPAT 131:144521

GI



I

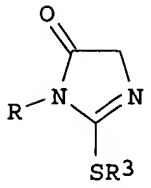
AB 2-Substituted-1-acyl-1,2-dihydroquinolines [I; R1 = CONH2, C(:NOH)NH2; R2 = (un)substituted Ph; R3, R4 = H, halogen, C1-6 alkyl, CF3], useful for increasing high d. lipoprotein cholesterol (HDL-cholesterol) concns. and for treating atherosclerotic conditions such as dyslipoproteinemias and coronary heart disease, are prepared Thus, quinoline was reacted with benzoyl chloride in the presence of AlCl3 and cyanated with Me3SiCN, producing 1-(benzoyl)-1,2-dihydroquinoline-2-carbonitrile, which was dissolved in acetone and reacted with sodium bicarbonate and 30% hydrogen peroxide, producing 1-(benzoyl)-1,2-dihydroquinoline-2-carboxamide (m.p. 169-171°), which demonstrated a 139% increase in the HDL-cholesterol level in the blood of rats when administered at 100 mg/kg per day (p.o.).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 40 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:152316 HCAPLUS
DOCUMENT NUMBER: 130:196654
TITLE: Preparation of 2-(substituted sulfanyl)-3,5-dihydro-imidazol-4-ones for increasing HDL blood levels
INVENTOR(S): **Elokdah, Hassan M.**; Sulkowski, Theodore S.; Strike, Donald P.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5877324	A	19990302	US 1996-754441	19961121

PRIORITY APPLN. INFO.: US 1996-754441 19961121
OTHER SOURCE(S): MARPAT 130:196654
GI



I

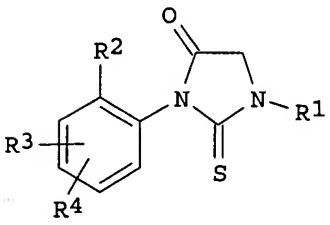
AB The title compds. [I; R = Ph or Ph optionally substituted with one or more groups selected from halo, alkyl, perfluoroalkyl, etc.; R3 = alkyl, aryl, arylalkyl] and their pharmaceutically acceptable salts, useful for increasing HDL blood levels, were prepared Thus, reaction of glycinamide with 4-fluorophenyl isothiocyanate followed by refluxing the resulting 2-[3-(4-fluorophenyl)thioureido]acetamide with EtI in EtOH afforded I [R = 4-FC6H4; R3 = Et] which showed 140% HDL cholesterol level increase at 80 mg/kg/day in 8 days treatment.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 41 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:53401 HCAPLUS
DOCUMENT NUMBER: 130:139338
TITLE: Preparation of 2-thioxo-imidazolidin-4-one derivatives for increasing blood serum HDL levels
INVENTOR(S): **Elokdah, Hassan M.**; Chai, Sie-Yearl; Sulkowski, Theodore S.; Strike, Donald P.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5861517	A	19990119	US 1996-749367	19961121

PRIORITY APPLN. INFO.: US 1996-749367 19961121
OTHER SOURCE(S): MARPAT 130:139338
GI



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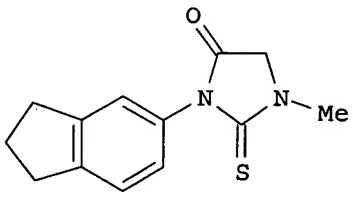


II

AB The title compds. [I; R1 = C1-6 alkyl, C2-6 alkenyl; R2 = C1-6 alkyl and R3, R4 = H, C1-6 alkyl; or R2 = H and R3R4 = ortho substituted

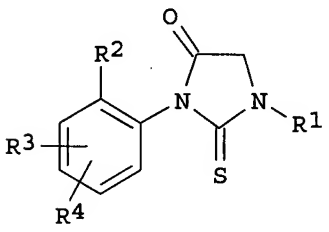
trimethylene or tetramethylene], useful for increasing blood serum HDL levels, were prepared Thus, reaction of sarcosine Et ester hydrochloride with indan-5-yl isothiocyanate in the presence of Et3N in CHCl3 afforded II which showed 112% HDL cholesterol level increase at 100 mg/kg.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 42 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:668042 HCAPLUS
DOCUMENT NUMBER: 129:302638
TITLE: Preparation of 2-thioxo-imidazolidin-4-ones for increasing blood serum HDL levels
INVENTOR(S): **Elokdah, Hassan M.**; Chai, Sie-Yearl; Sulkowski, Theodore S.; Strike, Donald P.
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5821372	A	19981013	US 1996-754451	19961121

PRIORITY APPLN. INFO.: US 1996-754451 19961121
OTHER SOURCE(S): MARPAT 129:302638
GI



I

AB The title compds. [I; R1 = C1-6 alkyl, C2-6 alkenyl, C6-10 aryl, C7-12 arylalkyl; R2 = C1-6 alkyl; R3 = halo; R4 = H; or R1 = C1-6 alkyl, allyl, Ph; R2 C1-3 alkyl; R3 = Cl; R4 = H], useful for increasing blood serum HDL levels, were prepared Thus, reaction of N-ethylglycine (preparation described) with 2-chloro-6-methylphenyl isothiocyanate in the presence of Et3N in CH2Cl2 afforded I [R1 = Et; R2 = Cl; R3 = 6-Me; R4 = H] which showed 222 % HDL cholesterol level increase.

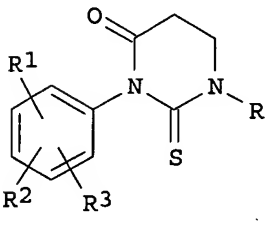
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 43 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:604660 HCAPLUS
DOCUMENT NUMBER: 129:245160
TITLE: Preparation of 2-thioxo-tetrahydropyrimidin-4-ones for treating atherosclerotic conditions
INVENTOR(S): Chai, Sie-Yearl; **Elokdah, Hassan M.**; Sulkowski, Theodore S.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S., 7 pp.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5807864	A	19980915	US 1997-807164	19970227

PRIORITY APPLN. INFO.: US 1997-807164 19970227
OTHER SOURCE(S): MARPAT 129:245160
GI



I

AB The title compds. [I; R = C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl; R1-R3 = H, halo, lower alkyl], which increase HDL cholesterol concentration and are useful in treating atherosclerotic conditions such as dyslipoproteinemias and coronary heart disease, were prepared Thus, reaction of 3-ethylaminopropionic acid with 2,6-dimethylphenyl isothiocyanate in the presence of Et3N in CH2Cl2 followed by treatment of a solution of the resulting 3-[3-(2,6-dimethylphenyl)-1-ethylthioureido]propionic acid in Me2CO with concentrate HCl afforded I [R = Et; R1 = 2-Me; R2 = 6-Me; R3 = H] which showed 184% HDL cholesterol level increase at 100 mg/kg/day (8 days treatment).
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

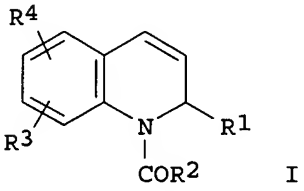
L27 ANSWER 44 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:543054 HCAPLUS
DOCUMENT NUMBER: 129:136105
TITLE: Preparation of 2-substituted-1-acyl-1,2-dihydroquinoline derivatives to increase HDL-cholesterol level.
INVENTOR(S): Babiak, John; **Elokdah, Hassan Mahmoud**; Miller, Christopher Paul; Sulkowski, Theodore Sylvester
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9833775	A1	19980806	WO 1998-US77	19980102

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9857310	A1	19980825	AU 1998-57310		19980102
ZA 9800834	A	19990802	ZA 1998-834		19980202
PRIORITY APPLN. INFO.:			US 1997-794692	A	19970203
			WO 1998-US77	W	19980102

OTHER SOURCE(S): MARPAT 129:136105
GI



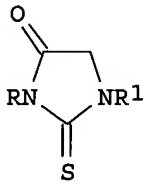
I

AB Title compds. [I; R1 = CONH2, C(:NOH)NH2; R2 = (halo-, alkyl-, or perfluoroalkoxy-substituted) Ph; R3, R4 = H, halo, alkyl, CF3; with provisos], were prepared Thus, quinoline, PhCOCl, and AlCl3 were stirred 10 min. in CH2Cl2; Me3SiCN was added dropwise and the mixture was stirred 4 h to give 1-benzoyl-1,2-dihydroquinoline-2-carbonitrile. The latter in acetone was treated with NaHCO3 and H2O2 to give 1-benzoyl-1,2-dihydroquinoline-2-carboxamide. The latter at 100 mg/kg/day orally in rats for 8 days increased HDL levels by 139%.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 45 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:493266 HCAPLUS
DOCUMENT NUMBER: 129:136167
TITLE: Preparation of 2-thioxoimidazolidin-4-one derivatives for increasing serum HDL levels.
INVENTOR(S): **Elokdah, Hassan M.**; Chai, Sie-Yearl; Sulkowski, Theodore S.; Strike, Donald P.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5783707	A	19980721	US 1996-754440	19961121
PRIORITY APPLN. INFO.:			US 1996-754440	19961121

OTHER SOURCE(S): MARPAT 129:136167
GI



I

AB Title compds. (I; R1 = alkyl; R = alkyl, naphthyl, benzhydryl, fluorophenylmethyl, phenethyl, 1-(fluorophenyl)ethyl, 5-chloro-2-methoxyphenyl, trifluoromethoxyphenyl, trifluoromethylphenyl, methylsulfanylphenyl, pyridyl), were prepared Thus, N-ethylglycine, 4-trifluoromethoxyphenyl isothiocyanate, and Et3N were refluxed in CH2Cl2 to give 1-ethyl-2-thioxo-3-(4-trifluoromethoxyphenyl)imidazolidin-4-one. The latter at 100 mg/kg orally in rats increased HDL cholesterol by 265%.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 46 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:397789 HCAPLUS
DOCUMENT NUMBER: 129:58784
TITLE: Use of 2-substituted benzimidazoles as smooth muscle cell proliferation inhibitors
INVENTOR(S): **Elokdah, Hassan M.**; Chai, Sie-Yearl; Sulkowski, Theodore S.
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5763473	A	19980609	US 1996-761694	19961206
TW 390876	B	20000521	TW 1996-85106313	19960528

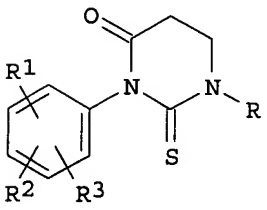
PRIORITY APPLN. INFO.: US 1996-761694 A 19961206
OTHER SOURCE(S): MARPAT 129:58784
AB The title compds. are effective for inhibiting platelet-derived growth factor-stimulated vascular smooth muscle cell proliferation. 1-(3,4-Dichlorobenzyl)-2-pyridin-2-yl-1H-benzimidazole (I) was prepared by treating 2-pyridin-2-yl-1H-benzimidazole with 3,4-dichlorobenzyl bromide. I was in vitro tested for antiproliferative activities using porcine aortic smooth muscle cells.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 47 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:618077 HCAPLUS
DOCUMENT NUMBER: 127:278205
TITLE: Preparation of 2-thioxotetrahydropyrimidin-4-ones for treating atherosclerotic conditions
INVENTOR(S): Chai, Sie-Yearl; **Elokdah, Hassan Mahmoud**; Sulkowski, Theodore Sylvester
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9732855	A1	19970912	WO 1997-US2281		19970212
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2247933	AA	19970912	CA 1997-2247933		19970212
AU 9721237	A1	19970922	AU 1997-21237		19970212
AU 707732	B2	19990715			
EP 885197	A1	19981223	EP 1997-906583		19970212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO					
CN 1217715	A	19990526	CN 1997-194335		19970212
BR 9708310	A	19990803	BR 1997-8310		19970212
JP 2000507926	T2	20000627	JP 1997-531771		19970212
TW 422840	B	20010221	TW 1997-86102010		19970220
ZA 9701911	A	19980907	ZA 1997-1911		19970305
PRIORITY APPLN. INFO.:			US 1996-12993P	P	19960307
			WO 1997-US2281	W	19970212

OTHER SOURCE(S): MARPAT 127:278205
GI



I

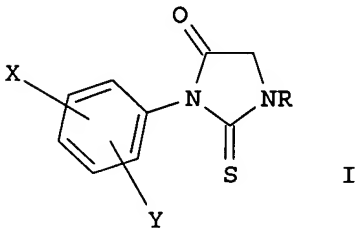
AB The title compds. [I; R = C1-6 alkyl, C2-6 alkenyl; R1-R3 = H, halo, lower alkyl], useful for increasing HDL cholesterol concentration and for treating atherosclerotic conditions such as dyslipoproteinemias and coronary heart disease, were prepared Thus, treatment of 3-chloropropionic acid with aqueous EtNH2 followed by reaction of the resulting 3-ethylaminopropionic acid with 2,6-dimethylphenyl isothiocyanate in the presence of Et3N in CH2Cl2, and treatment of 3-[3-(2,6-dimethylphenyl)-1-ethyl-thioureido]propionic acid with concentrate HCl in Me2CO afforded I [R = Et; R1 = 2-Me; R2 = H; R3 = 6-Me] which showed 184% HDL cholesterol level increase.

L27 ANSWER 48 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:599318 HCAPLUS
DOCUMENT NUMBER: 127:248113
TITLE: Preparation of 2-thioxoimidazolidin-4-one derivatives and their activity in increasing blood serum HDL

levels
INVENTOR(S): **Elokdah, Hassan M.**; Chai, Sie-yearl; Sulkowski, Theodore S.; Strike, Donald P.
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5663363	A	19970902	US 1996-754449	19961121
PRIORITY APPLN. INFO.:			US 1996-754449	19961121

OTHER SOURCE(S): MARPAT 127:248113
GI



I

AB The title compds. I (R = alkynyl; X, Y = alkyl, halo, perfluoroalkyl, perfluoroalkoxy; XY = ortho-substituted trimethylene or tetramethylene) were prepared and found to be useful for increasing blood serum HDL levels. E.g., reaction of BrCH2CO2Et and propargylamine gave Et (propargylamino)acetate, which was reacted with 2,6-C6H3NCS to give I (R = propargyl; X = 2-Me; Y = 6-Me) (II). II increased HDL cholesterol concentration
345% in a standard test.

L27 ANSWER 49 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:476253 HCAPLUS
DOCUMENT NUMBER: 127:95279
TITLE: Preparation of 2-(substituted sulfanyl)-3,5-dihydro-imidazol-4-ones for increasing HDL blood levels
INVENTOR(S): **Elokdah, Hassan Mahmoud**; Sulkowski, Theodore Sylvester; Strike, Donald Peter
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719931	A1	19970605	WO 1996-US19108	19961125

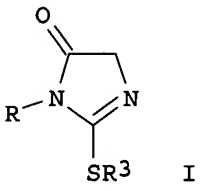
W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5599829	A	19970204	US 1995-563841		19951128
AU 9710634	A1	19970619	AU 1997-10634		19961125
EP 876354	A1	19981111	EP 1996-941513		19961125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, FI, RO					
JP 2000514401	T2	20001031	JP 1997-520711		19961125
PRIORITY APPLN. INFO.:			US 1995-563841	A	19951128
			US 1995-7653P	P	19951128
			WO 1996-US19108	W	19961125

OTHER SOURCE(S): CASREACT 127:95279; MARPAT 127:95279

GI



I

AB The title compds. [I; R = (un)substituted Ph; R3 = C1-6 alkyl, C6-10 aryl, C7-12 arylalkyl] and their salts, useful for increasing HDL blood levels in mammals, were prepared Thus, reaction of 4-fluorophenyl isothiocyanate with glycinamide in CHCl3 followed by cyclization of 2-[3-(4-fluorophenyl)thioureido]acetamide with EtI in EtOH afforded I [R = 4-FC6H4; R3 = Et] which showed 140% increase of HDL cholesterol level at 80 mg/kg/day after 8 days of treatment of male Sprague-Dawley rats.

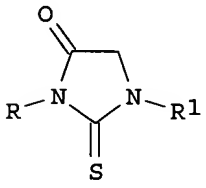
L27 ANSWER 50 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:473697 HCAPLUS
DOCUMENT NUMBER: 127:81453
TITLE: Preparation of 2-thioxo-imidazolidin-4-ones for increasing HDL cholesterol concentration
INVENTOR(S): **Elokdah, Hassan Mahmoud**; Chai, Sie-Yearl; Sulkowski, Theodore Sylvester; Strike, Donald Peter
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719932	A1	19970605	WO 1996-US19164	19961125
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5554607	A	19960910	US 1995-563325	19951128
TW 418195	B	20010111	TW 1996-85104367	19960412

TW 467903	B	20011211	TW 1996-85104368		19960412
AU 9711276	A1	19970619	AU 1997-11276		19961125
EP 876355	A1	19981111	EP 1996-942118		19961125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO					
JP 2000501100	T2	20000202	JP 1997-520724		19961125
PRIORITY APPLN. INFO.:			US 1995-563325	A	19951128
			US 1995-7654P	P	19951128
			US 1995-7658P	P	19951128
			US 1995-7661P	P	19951128
			US 1995-7665P	P	19951128
			US 1995-7666P	P	19951128
			WO 1996-US19164	W	19961125

OTHER SOURCE(S): MARPAT 127:81453
GI



I

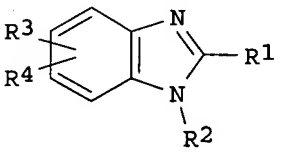
AB The title compds. [I; R = C1-6 alkyl, (un)substituted aromatic heterocyclyl containing N, O or S atoms, (un)substituted aryl, etc.; R1 = (un)substituted C6-10 aryl, alkyl, alkenyl, alkynyl], useful for increasing the HDL cholesterol concentration in the blood of a mammal, were prepared Thus, reaction of sarcosine Et ester hydrochloride with 5-chloro-2-methylphenyl isothiocyanate in the presence of Et3N in CHCl3 afforded I [R = 5-chloro-2-methylphenyl; R1 = Me] which showed 159% increase of HDL cholesterol level at 100 mg/kg.

L27 ANSWER 51 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:116576 HCAPLUS
DOCUMENT NUMBER: 126:131460
TITLE: Preparation of 2-substituted benzimidazoles as smooth muscle cell proliferation inhibitors
INVENTOR(S): **Elokdah, Hassan Mahmoud**; Sie-Yearl, Chai; Sulkowski, Theodore Sylvester
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640644	A1	19961219	WO 1996-US8374	19960603
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,				

	MR, NE, SN, TD, TG				
US 5654436		A	19970805	US 1995-477842	19950607
TW 386993		B	20000411	TW 1996-85106318	19960528
CA 2223962		AA	19961219	CA 1996-2223962	19960603
AU 9659683		A1	19961230	AU 1996-59683	19960603
AU 697295		B2	19981001		
EP 830344		A1	19980325	EP 1996-916977	19960603
EP 830344		B1	20011128		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1192204		A	19980902	CN 1996-195885	19960603
JP 11506752		T2	19990615	JP 1997-500993	19960603
BR 9608557		A	19990706	BR 1996-8557	19960603
NZ 309498		A	20000929	NZ 1996-309498	19960603
AT 209635		E	20011215	AT 1996-916977	19960603
ES 2165501		T3	20020316	ES 1996-916977	19960603
PT 830344		T	20020429	PT 1996-916977	19960603
ZA 9604622		A	19971204	ZA 1996-4622	19960604
PRIORITY APPLN. INFO.:				US 1995-477842 A	19950607
				WO 1996-US8374 W	19960603

OTHER SOURCE(S): CASREACT 126:131460; MARPAT 126:131460
GI



I

AB The title compds. [I; R1 = C1-6 alkyl, CF3, pyridinyl; R2 = H, C1-6 alkyl, (un)substituted C7-10 arylalkyl, etc.; R3, R4 = H, C1-6 alkyl, halo, NO2], useful as inhibitors of smooth muscle cell proliferation, were prepared Thus, treatment of Et butyroimidate.HCl with 4-nitro-1,2-phenylenediamine in EtOH followed by treatment of the resulting 2-propyl-5-nitroindole with NaH in DMF and addition of Et 4-(bromomethyl)benzoate afforded I [R1 = Pr; R2 = 4-EtOCOC6H4CH2; R3 = 5-NO2; R4 = H] which showed IC50 of 0.66 μM and 0.76 μM against porcine smooth muscle cell proliferation when cells were maximally stimulated with serum or PDGF, resp.

L27 ANSWER 52 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:116575 HCAPLUS
DOCUMENT NUMBER: 126:131459
TITLE: Preparation of 2-benzylthiobenzimidazoles as inhibitors of smooth muscle cell proliferation
INVENTOR(S): **Elokdah, Hassan Mahmoud**; Sie-Yearl, Chai; Sulkowski, Theodore Sylvester
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640645	A1	19961219	WO 1996-US8373	19960603

W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5684030	A	19971104	US 1995-482600	19950607
TW 411333	B	20001111	TW 1996-85106316	19960528
CA 2223939	AA	19961219	CA 1996-2223939	19960603
AU 9660303	A1	19961230	AU 1996-60303	19960603
AU 699503	B2	19981203		
EP 830346	A1	19980325	EP 1996-917920	19960603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1192207	A	19980902	CN 1996-195886	19960603
JP 11506751	T2	19990615	JP 1996-500992	19960603
BR 9609311	A	19990706	BR 1996-9311	19960603
ZA 9604621	A	19971204	ZA 1996-4621	19960604
PRIORITY APPLN. INFO.:			US 1995-482600 A	19950607
			WO 1996-US8373 W	19960603

OTHER SOURCE(S): MARPAT 126:131459
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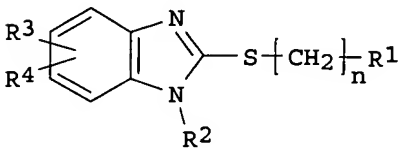

I

AB The title compds. [I; R1 = substituted Ph; R2 = H, C1-6 alkyl, etc.; R3, R4 = H, C1-6 alkyl, halo, NO2; n = 1-3], useful as inhibitors of smooth muscle cell proliferation, were prepared by reaction of the corresponding 1H-benzimidazol-2-thiol with the substituted benzyl bromide. Compound I.HCl [R1 = 4-MeOCOC6H4; R2-R4 = H] showed 1.53 μM and 3.74 μM against porcine smooth muscle cell proliferation when cell were maximally stimulated with serum or PDGF, resp.

L27 ANSWER 53 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:113845 HCAPLUS
DOCUMENT NUMBER: 126:195251
TITLE: 2-(substituted sulfanyl)-3,5-dihydro-imidazol-4-one derivatives, and preparation thereof, for increasing HDL cholesterol levels
INVENTOR(S): Sulkowski, Theodore S.; Strike, Donald P.; **Elokdah, Hassan M.**
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5599829	A	19970204	US 1995-563841	19951128
CA 2238812	AA	19970605	CA 1996-2238812	19961125

WO 9719931	A1	19970605	WO 1996-US19108		19961125
W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9710634	A1	19970619	AU 1997-10634		19961125
EP 876354	A1	19981111	EP 1996-941513		19961125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, FI, RO					
JP 2000514401	T2	20001031	JP 1997-520711		19961125
ZA 9609927	A	19980526	ZA 1996-9927		19961126
PRIORITY APPLN. INFO.:			US 1995-563841	A	19951128
			US 1995-7653P	P	19951128
			WO 1996-US19108	W	19961125

OTHER SOURCE(S): MARPAT 126:195251
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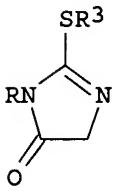

I

AB A method for increasing blood serum HDL cholesterol levels in a mammal comprises administering an effective amount of I (R = Ph, optionally substituted with ≥1 of halo, alkyl, perfluoroalkyl, alkoxy, perfluoroalkoxy, OH, alkanoyloxy, aroyloxy, arylalkanoyloxy; R3 = alkyl, aryl, or arylalkyl) or a pharmaceutically acceptable salt thereof. Preparation of 2-ethylsulfanyl-3-(4-fluorophenyl)-3,5-dihydroimidazol-4-one and 13 other compds. is described; HDL cholesterol-increasing activity for these compds. is reported.

L27 ANSWER 54 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:111148 HCAPLUS
DOCUMENT NUMBER: 126:117875
TITLE: Preparation of diheterocyclic acrylonitriles as smooth muscle cell proliferation inhibitors
INVENTOR(S): **Elokdah, Hassan Mahmoud**; Sie-Yearl, Chai; Sulkowski, Theodore Sylvester
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9639387	A1	19961212	WO 1996-US8376 19960603
W:	AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG		
US 5710164	A	19980120	US 1995-470603 19950606
CA 2223388	AA	19961212	CA 1996-2223388 19960603
AU 9660304	A1	19961224	AU 1996-60304 19960603
AU 711619	B2	19991021	
EP 835244	A1	19980415	EP 1996-917921 19960603
EP 835244	B1	20011205	
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI		
CN 1192202	A	19980902	CN 1996-195887 19960603
JP 11506754	T2	19990615	JP 1996-500995 19960603
BR 9608976	A	19990629	BR 1996-8976 19960603
NZ 309995	A	20000728	NZ 1996-309995 19960603
AT 210120	E	20011215	AT 1996-917921 19960603
ES 2166447	T3	20020416	ES 1996-917921 19960603
PT 835244	T	20020429	PT 1996-917921 19960603
ZA 9604620	A	19971204	ZA 1996-4620 19960604
PRIORITY APPLN. INFO.:			US 1995-470603 A 19950606
			WO 1996-US8376 W 19960603

OTHER SOURCE(S): CASREACT 126:117875; MARPAT 126:117875

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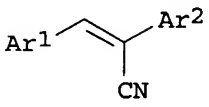


I

AB The title compds. [I; Ar1, Ar2 = pyridinyl, quinolinyl, dihydro-1,4-benzodioxinyl, pyrrolyl, azaindolyl, carbazolyl], or their salts, useful as inhibitors of smooth muscle cell proliferation, were prepared Thus, condensation of 3-pyridylacetonitrile with 4-pyridylcarboxaldehyde in the presence of NaOMe/MeOH in EtOH afforded 48% (Z)-I [Ar1 = 4-pyridinyl; Ar2 = 3-pyridinyl] which showed IC50 of 1.159 and 0.346 μM against porcine smooth muscle cell proliferation when cells were maximally stimulated with serum or PDGF, resp.

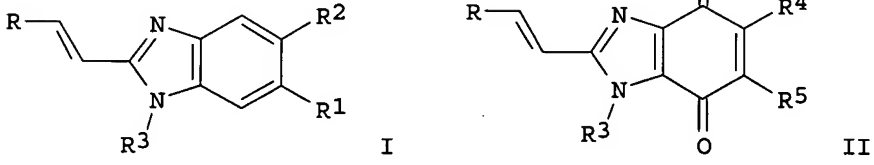
L27 ANSWER 55 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1997:101668 HCAPLUS
DOCUMENT NUMBER:	126:117976
TITLE:	Preparation of styrylbenzimidazoles as inhibitors of smooth muscle cell proliferation
INVENTOR(S):	Chai, Sie-yearl; **Elokdah, Hassan Mahmoud**; Sulkowski, Theodore Sylvester
PATENT ASSIGNEE(S):	American Home Products Corporation, USA
SOURCE:	PCT Int. Appl., 35 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639391	A1	19961212	WO 1996-US8375	19960603
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6444694	B1	20020903	US 1995-468271	19950606
CA 2223585	AA	19961212	CA 1996-2223585	19960603
AU 9659684	A1	19961224	AU 1996-59684	19960603
AU 711965	B2	19991028		
EP 830345	A1	19980325	EP 1996-916978	19960603
EP 830345	B1	20010905		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1192206	A	19980902	CN 1996-195860	19960603
BR 9609153	A	19990504	BR 1996-9153	19960603
JP 11506753	T2	19990615	JP 1997-500994	19960603
NZ 309499	A	20000825	NZ 1996-309499	19960603
AT 205196	E	20010915	AT 1996-916978	19960603
ES 2162063	T3	20011216	ES 1996-916978	19960603
PT 830345	T	20020130	PT 1996-916978	19960603
ZA 9604693	A	19971205	ZA 1996-4693	19960605
PRIORITY APPLN. INFO.:			US 1995-468271 A	19950606
			WO 1996-US8375 W	19960603

OTHER SOURCE(S): CASREACT 126:117976; MARPAT 126:117976

GI



I II

AB The title compds. [I and II; R = (un)substituted Ph, furyl, pyridyl, quinolinyl; R1, R2 = H, halo, alkyl, etc.; R3 = H, alkyl, aryl, arylalkyl; R4, R5= H, alkyl] or their salts, useful as inhibitors of smooth muscle cell proliferation, were prepared Thus, treatment of 3,4-dimethoxycinnamonitrile with HCl gaseous in EtOH followed by reaction of 1,2-phenylenediamine with the resulting Me (3,4-dimethoxy)cinnamoimidate.HCl in MeOH afforded 67% I which showed IC50 of 5.91 μM and 4.1 μM against porcine smooth muscle cell proliferation when cells were maximally stimulated with serum or PDGF, resp.

L27 ANSWER 56 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:97265 HCAPLUS

DOCUMENT NUMBER: 126:117977

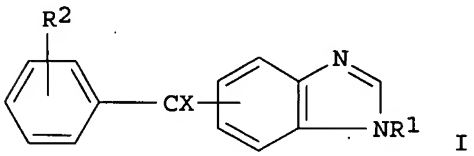
TITLE: Preparation of benzoylbenzimidazoles and related compounds as inhibitors of smooth muscle cell proliferation.

INVENTOR(S): **Elokdah, Hassan Mahmoud**; Sie-Yearl, Chai; Sulkowski, Theodore Sylvester

PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639390	A1	19961212	WO 1996-US8353	19960603
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, FI, GE, HU, IL, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6288100	B1	20010911	US 1995-468482	19950606
CA 2223393	AA	19961212	CA 1996-2223393	19960603
AU 9659673	A1	19961224	AU 1996-59673	19960603
AU 713043	B2	19991125		
EP 830343	A1	19980325	EP 1996-916965	19960603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1192205	A	19980902	CN 1996-195888	19960603
BR 9609365	A	19990518	BR 1996-9365	19960603
JP 11506749	T2	19990615	JP 1996-500980	19960603
ZA 9604692	A	19971205	ZA 1996-4692	19960605
PRIORITY APPLN. INFO.:			US 1995-468482 A	19950606
			WO 1996-US8353 W	19960603

OTHER SOURCE(S): MARPAT 126:117977
GI



I

AB Title compds. [I; R = alkyl, (substituted) Ph, PhCH2; R2 = H, halo, alkoxy, alkyl; R1 = H, alkyl, aryl, arylalkyl, substituted PhCH2; X = O, (H,OH)], were prepared Thus, Ph (2-propyl-1H-benzimidazol-5-yl)methanone (preparation given) in DMF was treated with NaH and then with Me 4-bromomethylbenzoate and the mixture was stirred 4 h to give 4-(5-benzoyl-2-propylbenzimidazol-1-ylmethyl)benzoic acid Me ester. This was converted to the Et ester, which showed IC50 = 1.04 μM for inhibition of porcine smooth muscle cell proliferation.

L27 ANSWER 57 OF 57 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:580563 HCAPLUS
DOCUMENT NUMBER: 125:275874
TITLE: Use of 2-thioxo-imidazolidin-4-one derivatives in the treatment of atherosclerosis
INVENTOR(S): **Elokdah, Hassan M.**; Chai, Sie-yearl; Sulkowski, Theodore S.; Strike, Donald P.

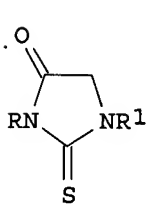
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S., 15 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5554607	A	19960910	US 1995-563325	19951128
CA 2238762	AA	19970605	CA 1996-2238762	19961125
WO 9719932	A1	19970605	WO 1996-US19164	19961125
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9711276	A1	19970619	AU 1997-11276	19961125
EP 876355	A1	19981111	EP 1996-942118	19961125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2000501100	T2	20000202	JP 1997-520724	19961125
ZA 9609973	A	19980527	ZA 1996-9973	19961127

PRIORITY APPLN. INFO.:

US 1995-563325	A	19951128
US 1995-7654P	P	19951128
US 1995-7658P	P	19951128
US 1995-7661P	P	19951128
US 1995-7665P	P	19951128
US 1995-7666P	P	19951128
WO 1996-US19164	W	19961125

OTHER SOURCE(S): MARPAT 125:275874
GI



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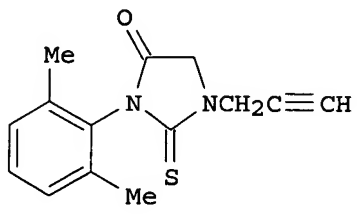

II

AB A method for increasing the HDL cholesterol concentration in the blood of a mammal comprises administration of a title compound I [R = alkyl, (un)substituted aromatic N, O or S heterocycle, aryl, aralkyl, benzhydryl, or indanyl (in which the substituents are 1-3 members selected from alkyl, alkoxy, alkylthio, alkenyl, alkynyl, halo, perfluoroalkyl, perfluoroalkoxy, or OH); R1 = alk(en/yn)yl, (un)substituted aryl (in which the substituents are 1-3 members selected from alk(en/yn)yl, alkoxy, alkylthio, halo, perfluoroalkyl, perfluoroalkoxy, or OH)]. Over 60 compds. were prepared For instance, reaction of BrCH2CO2Et with HC.tplbond.CCH2NH2 in Et2O at 0° to room temperature gave HC.tplbond.CCH2NHCH2CO2Et, which reacted with 2,6-dimethylphenyl isothiocyanate and Et3N in refluxing CH2Cl2 to give title compound II. At